Primer of Geriatric Urology

Second Edition

Thomas J. Guzzo
George W. Drach
Alan J. Wein
Editors

Springer

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Preface

The American population over the age of 65 will grow greatly in the next two decades. The US Census Bureau has estimated that by 2030, 20 % (approximately 72 million people) of the US population will be in this group. Currently, one in every ten individuals in the world is over 60 years of age; by 2050, this number will double to 1 in 5! Additionally, due to improvement in medical care, elderly individuals are living longer. In 2004, the median life expectancy for an individual reaching age 65 reached 17.1 years and age 75, 10.7 years. While many health-care specialists will feel the impact of this growing elderly population, few will be more affected than those in the field of urology. Many urologic disorders have an increased prevalence among the elderly: nearly 50 % of outpatients and over 60 % of surgical/procedural patients encountered in US urologic practice are over the age of 65 years.

As medical students on our pediatric rotations, we learn early on that children are not "little adults." The obvious wisdom of this saying is that pediatric patients have a unique physiology and pathophysiology that is not necessarily transferable from what we learn on the adult wards. One can also say the same for our geriatric patient population. Borrowing this phrase from our pediatric colleagues, it is not just as simple as "they are older adults." The elderly urology patient merits special assessment on several fronts. Many nonoperative urologic conditions are treated with medications which can affect cognition and/or interact with other daily medications. Urinary issues, such as incontinence or frequency, can lead to significant morbidity in the functionally impaired, leading to falls. Surgical intervention is common for urologic disease, both oncologic and benign, and must be carefully considered in the geriatric patient.

The second edition of this book is intended to provide a review of the demographics of our aging urologic population and their unique needs. Like the first edition, this book covers medical issues particular to the elderly that must be considered in the initial evaluation of the aging patient, and follows this with practical suggestions in development of the management plan, whether by medication or invasive procedure. Common complications (and their management) encountered in the treatment of elderly inpatients are also covered. Important aspects of continuity of care are also included, such as appropriate use of adjunctive services and the

urologic aspects of nursing home care. Finally, specific urologic disease processes in the elderly population are reviewed including urologic oncology, lower urinary tract symptoms, and sexual dysfunction. Each chapter has been updated from the initial edition to reflect the current literature and medical practice.

We believe the second edition of this book will be useful to anyone who is involved in the care of geriatric patients including medical students, residents, general practitioners, internists, and urologists. This book is not intended to be an exhaustive review of urology or geriatrics but rather an easy to use, practical, and rationale guide to common urologic management problems in the geriatric population. The chapters are purposefully concise so that health-care providers can use the information contained within the book "on the fly": either on rounds or while seeing patients in the office. It is our hope that this book will aid the reader to better address some of the unique needs of this growing patient population.

Philadelphia, PA, USA Thomas J. Guzzo, MD, MPH

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Chapter 1
Introduction: Aging

Abdo E. Kabarriti and George W. Drach

We created this text for you, the urologic resident, practicing urologist and urologic surgeon, so that you would encounter fewer troubles as you care for your elderly patients. We know that in many instances you rely on other physicians or medical personnel to assist you in this geriatric care, but we believe that if you can increase your level of knowledge in evaluation and management of the older patient slightly at the time of your first encounter that you will obtain a smoother course throughout the duration of subsequent management and care of your patient. In addition to this text, a compact major source of reference material regarding geriatric care by specialists other than geriatricians can be found in the manual: "Geriatrics at Your Fingertips" hereafter referred to as GAYF. It is published by the American Geriatrics Society and can be accessed at http://www.geriatricsatyour.fingertips.org [1].

Demography in the USA

If you treat mostly adult patients, look into your waiting room 1 day and you will see a large number of gray-haired patients. Urologists serve a large number of Medicare beneficiaries (Fig. 1.1) and the number of Medicare beneficiaries is only expected to grow (Table 1.1). In fact, in 2012, the only surgical specialties to serve more Medicare patients were ophthalmology and orthopedic surgery. In one model,

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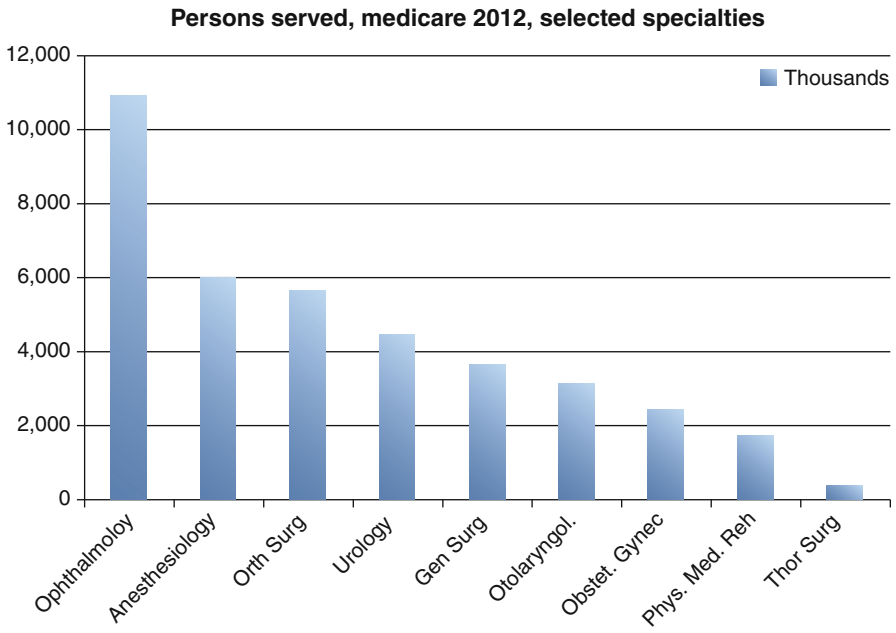

Fig. 1.1 Number of persons served by selected surgical and related specialties in year 2012

Table 1.1 Projected Medicare beneficiaries by millions with percent of population projected to be Medicare beneficiaries

Medicare beneficiaries	Million	% of population
2010	47.7	15
2020	64.3	19
2030	81.5	23
2040	88.9	23

Source: 2013 Annual report of the board of trustees of the federal hospital insurance and federal supplementary medical insurance trust funds

urology services were projected to increase by 17 % by 2025, surpassed only by cardiology and rheumatology [2].

Your elderly urologic patients merit special assessment on several fronts. Many nonoperative urologic conditions, such as lower urinary tract symptoms, require treatment with medications that can affect cognition and/or interact with other daily medications [1]. Urinary afflictions such as frequency, urgency, and incontinence contribute to non-urologic morbidity because of requirement for movement and result in falls. The need to arise at night for voiding (nocturia) also leads to increased risk of falls in the darkened environment. Older patients' needs differ because processes of aging make them different from those younger than 65 years. Why? Because the physiology of aging generates changes that cause the elderly to have less physiological strength in many organ systems. Perhaps one of the best illustrations of these changes is summarized in Fig. 1.2 [3]. Note that renal

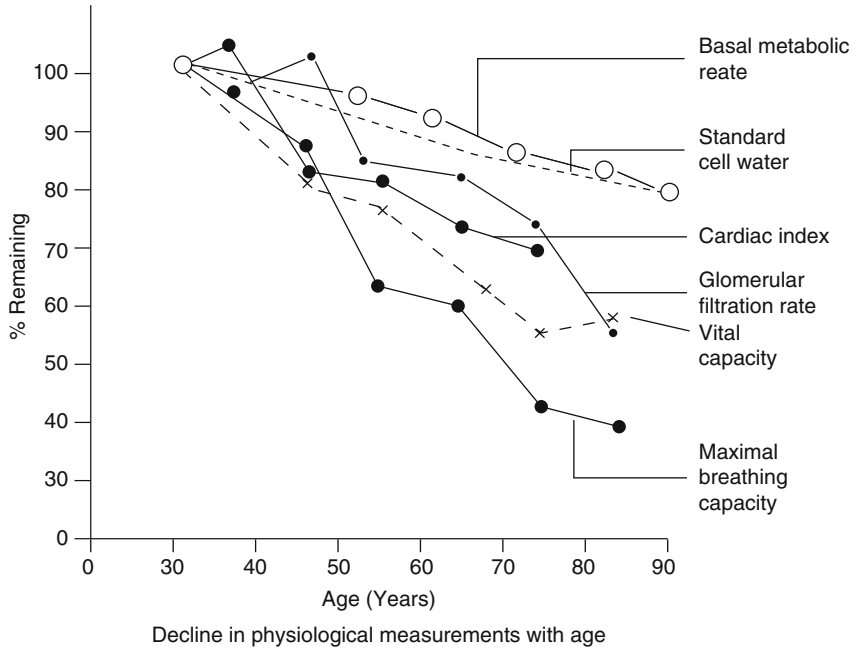

Fig. 1.2 Graphic depiction of deterioration of various body systems as one ages

function decreases to 60 % of normal by age 80, cardiac function by 30 % and pulmonary function by 50–60 %. Some geriatricians term this loss of reserve function in body systems as "homeostenosis" or lack of ability to respond adequately to external stresses, versus the usual beneficial response of "homeostasis" [4]. It is this inability to respond to stress that causes the increased risk levels that one tries to include in various co-morbidity classifications. And in addition to consideration of the usual disease conditions that one considers dangerous (hypertension, cardiovascular disease, pulmonary disease, diabetes, etc.), there are a number of additional topics that pertain to the aged patient, termed "geriatric syndromes" (Table 1.2) [5].

Yet many patients over age 75 or 80 retain excellent physiologic function through a combination of physical conditioning and lack of chronic disease. Hence, it becomes critical to evaluate the older patient on a basis of physiologic rather than chronologic age. Several methods to predict likelihood of survival in years (remaining life span) or of operative risk exist. These include the Charlson Index (Table 1.3) and the Anesthesia Society of America (ASA) classification (Table 1.4) [6]. Use of these concepts of co-morbidity is brought together in the South Florida Treatment Algorithm (Table 1.5) [7]. In general, for patients with no co-morbidities, one estimates years of life remaining by using predictive tables (Table 1.6). Due to improvements in general health and medical care, the 2013 median life expectancy for an individual reaching age 65 was 19.3 years and at age 75 reached 12.2 years. And, as of 2010, if the age achieved is 85, there is still an expectancy of 6.5 years.

Table 1.2 Geriatric syndromes

Deconditioning
Delirium
Dementia
Elder abuse
Falls/difficulty walking
Frailty
Malnutrition
Difficulty swallowing
Palliative care/end of life
Polypharmacy
Pressure ulcers
Transitional care
Urinary incontinence
Sleep disorders
Vision and hearing impairments
Osteoporosis

Table 1.3 Charlson comorbidity index

Points	
1	Myocardial infarction
	Congestive heart failure
	Peripheral vascular disease
	Cerebrovascular disease
	Dementia
	COPD
	Connective tissue disease
	Peptic ulcer disease
	Diabetes mellitus without end-organ damage
	Age 50–59 years
2	Hemiplegia
	Moderate or severe renal disease
	Diabetes mellitus with end-organ damage
	Tumor without metastasis
	Leukemia (acute or chronic)
	Lymphoma
	Age 60–69 years
3	Moderate or severe liver disease
	Age 70–79 years
6	Metastatic solid tumor
	AIDS

Urologists will be faced with the inevitable results of this growth of the elderly population, because we care for many elderly in our outpatient and inpatient practices. And, you probably had little or no previous education in the specifics of care of our older patients while in medical school or residency. Perhaps you could say

Table 1.4 American Society of Anesthesiologists physical status classification system

1	A normal healthy patient
2	A patient with mild systemic disease
3	A patient with severe systemic disease
4	A patient with severe systemic disease that is a constant threat to life
5	A moribund patient who is not expected to survive without the operation
6	A declared brain-dead patient whose organs are being removed for donor purposes

Data from American Society of Anesthesiologists

Table 1.5 Concepts of adaption in treatment for the elderly

Impact of co-morbidities on life expectancy of elderly patient Basic principle: will you extend life if you treat/operate on this patient?		
Health status	Life expectancy	What to offer
Healthy with no co-morbidities	At age 65–17 years At age 85–7 years	Normal treatment regimen
Two or fewer co-morbidites	Less than healthy patient	Regimen adapted to co-morbidites
Three or more co-morbidities	Much less than healthy patient	Regimen to provide comfort and/or palliation

Adapted from Lichtman

Table 1.6 Estimation of mean remaining lifetimes for individuals at birth, 65, and 75 years of age for the year 2013

	Life expectancy in years		
Age in 2013 (years)	Both sexes	Male	Female
0	78.8	76.4	81.2
65	19.3	17.9	20.5
75	12.2	11.2	12.9

Source: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Health Statistics

that you did learn such things because you've had "on the job training," but indeed that is not adequate for geriatrics just as it is not adequate for pediatrics.

Many elderly urologic patients merit special assessment on several fronts. As noted above, many nonoperative urologic conditions (such as lower urinary tract symptoms) require medications that can affect cognition or interact with other daily medications. Which are these? Urinary incontinence or urgency and frequency can lead to related morbidities such as falls or loss of necessary sleep. Have these points already been considered? When surgical intervention is contemplated, critical elements such as degree of normal cognition, level of frailty, living conditions and sites of postsurgical aftercare must be considered. Do you know that in 2013, over 1/3 of

all noninstitutionalized older women live by themselves and by age 75, 46 % live alone [8]! Who takes care of them after surgical intervention?

Having, I believe, proved to you that most adult urologists have a significant geriatric practice, the next goal is to present to you the basics of effective evaluation and to prepare for effective management of the geriatric patient. Our next chapter will introduce you to the major additional points needed in the evaluation of the older patient. Thereafter you will be introduced to the major approaches you may take toward the elderly patient in your office procedures. Subsequent chapters will discuss medical therapy and procedural therapy. Then will follow a consideration of those complications peculiar to the older patient. Next, you will be exposed to use of adjunctive services and, possible, nursing home adjuncts. Finally, there will be coverage of those specific entities of geriatric urology: cancer, lower urinary tract symptoms, and sexuality.

Our purpose is to improve your care of the geriatric patient, to lubricate and ease your office procedures in the management of these patients and to promote effective decision making during hospitalization and treatment of the elderly patient, especially those considered to be the frail elderly. This will not be a comprehensive text, but as the title says, a "Primer" to help you gain additional fundamental knowledge that is important in the care of your geriatric patient.

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Chapter 2
Approach to the Elderly Patient: Evaluation

Abdo E. Kabarriti and George W. Drach

Geriatric Urology adds a number of specific requirements to your knowledge and skill set in the evaluation and management of the elderly patient. One list summarizes a number of geriatric syndromes [1] that are unique to care of the elderly patient (Table 2.1). Including these domains into your original evaluation takes very little extra time, but it does take some extra attention. Throughout this Chapter, we will be referring to a small text published by the American Geriatrics Society entitled "Geriatrics at Your Fingertips [2]" (GAYF). It is available online or in print at http://geriatricsatyourfingertips.org/ and it is a recommended addition to your office library for your care of geriatric patients.

Several steps must be added to the usual initial history and physical assessment of your geriatric patient that will improve your ability to care for them as you proceed to your management phase. Your first additional step will be to determine the patient's communication status. Is there evidence or history of decreased hearing or vision? About 60 % of older patients have difficulty with one or the other or both senses [3]. What is their medical literacy level? Again, at least 1/4 of patients have a lack of education or basic lack of understanding of common medical terms [4]. And with the growing number of legal or illegal immigrants into the USA, urologists are likely to see many persons from foreign countries with their own specific cultural prejudices regarding medical care. Often, a family member acts as the interpreter— but the patient may not wish to divulge all of their history through that

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Table 2.1 Geriatric syndromes

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Dementia
Elder abuse
Falls/Difficulty walking
Frailty
Malnutrition
Difficulty swallowing
Palliative care/end of life
Polypharmacy
Pressure ulcers
Transitional care
Urinary incontinence
Sleep disorders
Vision and hearing impairments
Osteoporosis

person. Accordingly, your initial record should simply record at the outset these three points: adequacy of senses, medical literacy, and cultural background. Thereafter, if you proceed with various treatment plans you can account for these special needs, e.g., being sure to have hearing aids available in the ICU after surgery.

During acquisition of the history, some special inquiries must be added. One of the most important regards questions about present prescription medications as well as all over-the-counter (OTC) drugs including supplements, vitamins, and herbal/alternative therapies. Many elderly patients use such medications. For example, ingestion of significant amounts of ginseng can lead to bleeding complications [5, 6]. Most older persons take multiple prescription medications which is discussed in a later chapter.

Additional questions must include the functional capacity of the individual. Can they still stoop, lift, reach, grasp, and walk adequately? About 28 % of Medicare patients express some difficulty with these activities Fig. 2.1 [3]. After you have undergone major abdominal surgery, grip strength status may not be recovered even 6 months after surgery in many patients [7]. If these functional abilities are limited before surgery, they will likely never be recovered, and your patient will require help to get the jar off the upper shelf and then open it. Also, many Medicare patients express difficulty with one or more of the Activities of Daily Living (ADL) such as toileting, bathing, eating, dressing, grooming, or (as noted above) walking (Fig. 2.2) [8]. A quick ADL assessment will define where help may be needed. If and when discharge plans are to be made, the number of ADL disabilities will help determine the discharge site (See Chap. 7). And finally, one must assess and record the Instrumental Activities of Daily Living [9] (IADL), so named because they require some type of tool or instrument to accomplish them. They are phoning, shopping, cooking, cleaning, laundering, and traveling as the elderly are more likely to have

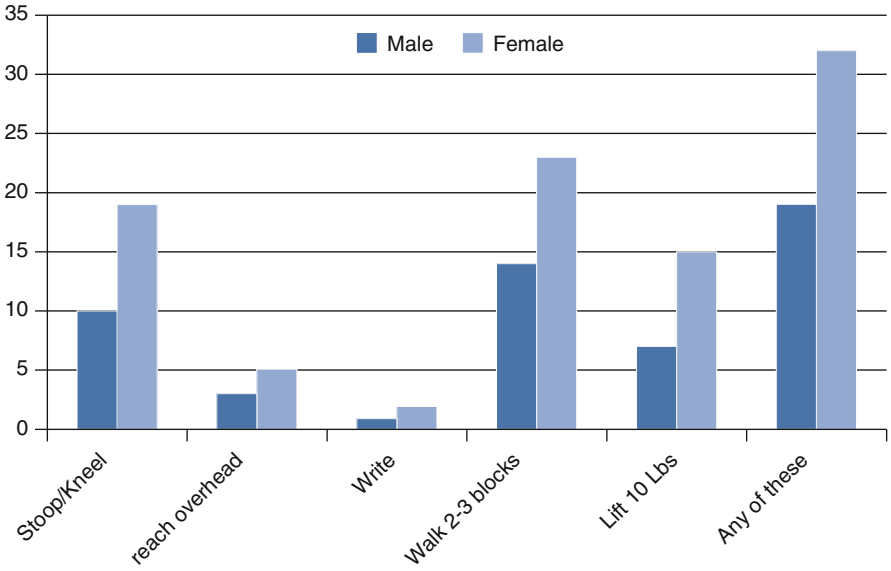

Fig. 2.1 Percentage of Medicare beneficiaries who are unable to perform certain physical functions (Source: Federal interagency forum on aging-related statistics. Older Americans 2010: key indicators of well-being)

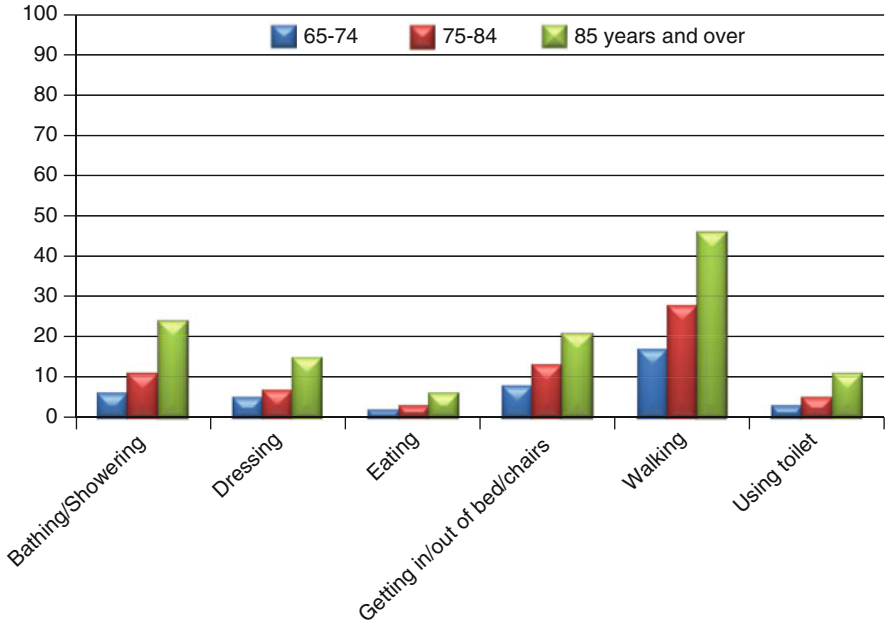

Fig. 2.2 Percent of persons with limitations of select activities of daily living by age group in 2010

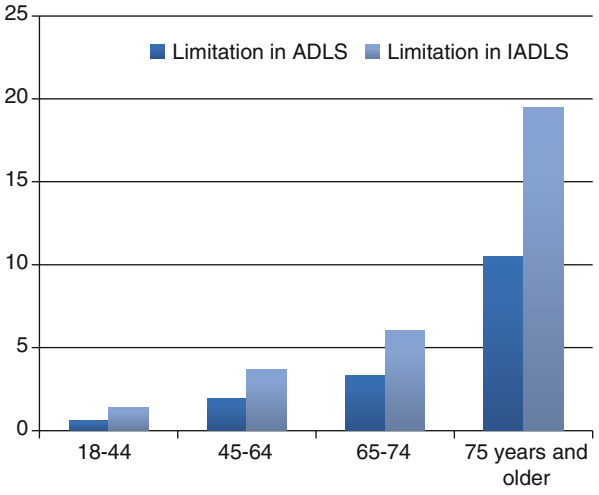

Fig. 2.3 Percent of persons with limitations in activities of daily living and instrumental activities of living by age group in 2012

limitations with these activities (Fig. 2.3) [10]. For example, can the patient phone the dispatcher to order a cab to go shopping for food and soap? Noting these points may seem onerous, but recording them during your initial encounter will save much time later in your course of care for the patient.

Estimating and maintaining functional status for your patient becomes one of the most critical portions of your geriatric care. In the past, Forciea and I [5] have indicated that "No element of the preoperative examination of the older patient is more predictive of perioperative morbidity and mortality than functional ability." If, for example, you doubt the patient's ability to "get about," you can easily include a brief "Get-Up-and-Go" test [10] into your office activities (Table 2.2). This might take one of your office staff 2–3 min, but doing so will save you many hours if your patient cannot ambulate after surgery [11, 12].

As you go through these prior points in acquiring the history, you will be making observations about the patient's mental status and likely competency. At some point you may begin to question the patient's mental state or the companion/caregiver may mention concern about the patient's mental ability. Two simple helps can be applied. First, the Mini-Mental Status examination can be done [13] (again by your trained office staff) (Table 2.2). It is available in GAYF also. If this suggests problems, you may want to request additional geriatric and/or psychiatric examinations. Second, it you question the patient's understanding of your descriptions of their problem or of your treatment plan, it is helpful to use the "repeat back" system. This requires that the patient "repeat back" to you so that you can understand what you have offered [14]. If you judge that the "repeat back" is adequate, it is useful to enter into the record your written confirming note. Then the patient and possible companion can sign along with you (this is still possible during these days of electronic records). If the above two processes create for you continued concern in the absence of a spouse or guardian, then it is advisable to determine whether someone is or could be created as a guardian for your patient. Every county in the USA has an

Table 2.2 Functional and cognitive status assessments

	Assessment	Interpretation
Functional Status	*Get-up-and go test* Patient must: 1. Rise from a chair without using arms for boost or support 2. Walk 10 feet in a straight line 3. Turn around 4. Walk back to chair 5. Sit down without using arms for support	Observations: Are there any unusual movements? Balanced walking? Any weaving or hesitancy? Regular steps without difficulty? If no problems, mobility function should be adequate Some prefer to time test: if time <15 s test is good [11]
Cognitive status	*Mini-mental status evaluation (GAYF)* 1. With patient's attention, mention three unrelated words that are to be remembered 2. Ask the patient to draw a clock face with a specific time, such as 8:20 3. Have the patient repeat the three words in 1. Above	*Grading* : Give one point for each word remembered. Give 2 points for a normal clock face 0–2 points suspicious for dementia

office on aging that your patient's family or companion can contact for advice on this subject. Their office names may be unusual. As an example, for Philadelphia, the office is titled the "Philadelphia Corporation for Aging," but services for the elderly are available.

About 1/3rd of all elderly patients who present with an urgent or emergent problem will manifest some degree of malnutrition [15]. As we all know, these patients heal poorly, have poor immune response, and encounter many more postoperative complications. Some initial hints may appear: weight loss of >10 lb in the past 6 months, body-mass-index (BMI) of under 22 or serum albumen of less than 3.0 on multi-test chemical panel (GAYF). Treatments by means of intravenous alimentation and so forth may result in some improvement [16]. If time allows, the production of improved nutrition in conjunction with a trained dietician provides the best resolution. However, if intervention is urgent, one must caution the family/friends that the risk is much higher for that patient. Under-nutrition, for example, clearly enhances the likelihood of pressure ulcers [17].

As mentioned above, many elderly single women in the USA live alone. In 2012, about 11.8 million (28 %) of all noninstitutionalized older persons lived alone. Women were more likely to live alone with 36 % of women living alone compared to 19 % of older men. The proportion living alone only increased with advanced age as 46 % of women aged 75 and over lived alone [8]. What is your patient's living and social environment? Who will care for them after their procedure? Do they have easy access to a kitchen or toilet and a bedroom on a single floor or are many steps up or down required? So knowledge of living arrangements and social status become important in your initial records, especially if you are to progress to some major procedural/operative intervention Here again, if you have significant questions

Table 2.3 Evaluation of the geriatric patient

Considerations in the initial evaluation of the geriatric patient
Communication status:
Decreased hearing or vision
Medical literacy level
Cultural or language barriers
Polypharmacy
Prescription medications, OTC drugs, supplements, and alternative therapies
Functional status:
Physical capacities: stooping, lifting, reaching, grasping, and walking
Activities of Daily Living (ADL): toilet, bathe, eat, dress, groom, walk
Instrumental Activities of Daily Living (IADL): phone, shop, cook, tidy up, launder, travel
Cognitive status and competency
Nutritional status
Living arrangements and social status
Legal documents

about the home situation, you might obtain assistance from a nearby social service group, often found in your local hospital or in conjunction with the county aging office, mentioned above.

Although frequently mentioned in popular literature, it is surprising how many elderly patients have not initiated their Living Will or Health Care Power of Attorney (HCPOA) or Physicians Orders for Life Sustaining Treatment (POLST) (GAYF). Availability of such legal documents should be noted, and if not done, your patient should be encouraged to accomplish this before even the simplest of procedures.

So now we have covered most of the additional historical knowledge that you must obtain in order to do your best for your geriatric urology patient. These points are summarized in Table 2.3 as a quick reminder. Cudennec et al. [18] have called completion of these steps a "Simplified Geriatric Assessment," and they found it to be an "important aid to decision making in the management of elderly patients with bronchial cancer." It seems that it can be just as useful in urology. We will assume that your usual general questions and specific urologic system inquiries for voiding difficulty, sexual function, presence or absence of incontinence, histories of urologic diseases such as infection, calculi, or carcinoma have been completed.

Next, one performs the appropriate physical examination for the patient. This may be a head-to-toe complete physical examination or a system limited physical, depending on your analysis of the chief complaint. In addition to your usual observations, some general conditions may be noted and important in your future care of the patient. These include evidence of frailty, or "a transitional state in the dynamic progression from robustness to functional decline." It is further characterized by the fact that no single system is altered, but multiple systems are involved [19, 20].

Table 2.4 Identifying need for preoperative testing

Indications for preoperative testing	
Diagnostic efficacy	Does the test correctly identify abnormalities?
Diagnostic effectiveness	Would the test change your diagnosis?
Therapeutic efficacy	Would the test change your management?
Therapeutic effectiveness	Would the test change the patient's outcome?

Adapted from Hepner DL [21]

Table 2.5 Medical comorbidities requiring consultations

Preoperative consultation recommended for patients with these conditions
Recent myocardial disease/angina
Arrythmias
Aortic stenosis
Chronic lung disease
Renal or hepatic failure
Diabetes mellitus
Dementia or history of delirium

However, performance of the above thorough history and examination will uncover the clues necessary to diagnose frailty: appearance not consistent with age, poor nutrition, poor subjective health rating, poor mental and physical performance, decreased sensory status and inadequate current living and care levels. Frail patients demonstrate a much higher risk of morbidity and mortality after any intervention. Other geriatric syndromes that may be noted on your examination (Table 2.1) are osteoporosis, arthritis, or limited mobility. These may strongly impact your ability to position the patient for various procedures. An inquiry about falls within the past year may provide a hint about difficulty in ambulation and balance and enable you to initiate special protections if the patient is to be hospitalized. Of course, once you have covered these points in your history and physical examination, you will be looking for additional laboratory tests that might help you beyond the usual CBC and urinalysis. Some no longer recommend "routine" preoperative laboratory testing, but indicate that your requests should be based on your expectations of need [21], as illustrated in Table 2.4. Then, if your suspicions of potential difficulty increase after the initial history, physical examination and preliminary laboratory tests, you may feel the need for additional consultation. Table 2.5 depicts those conditions that should be evaluated by a specialist in that area (GAYF). But other suspicions should engender other consultations. Or perhaps a "Comprehensive Geriatric Assessment" may be in order, if you have a geriatrician nearby [22]. However, if, at this point you feel that you find your patient healthy and with minimal morbidity for his or her age, you may feel con fi dent that you have performed your evaluation with the necessary added geriatric components and proceed with some degree of confidence. In our next chapter, you will be reminded of approaches to the specifics of urologic office procedures in the elderly patient.

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Chapter 3
Urologic Office Procedures

Siobhan M. Hartigan and Ariana L. Smith

Positioning for Office Procedures

Simple procedures such as catheterizations and flexible cystoscopy may be performed in the supine position in men and in the "frog-legged" position in women. More complex office procedures with rigid cystoscopy will require the patient to be placed in the lithotomy position. In the lithotomy position, the patient is supine with their buttocks at the end of the exam table, the legs are placed in stirrups such that the angle of flexion at the hips and knees are no more than 90°, and the hips are abducted generally no more than 30°. Examples of the "standard" and "low" lithotomy position are shown in Fig. 3.1. Lithotomy and low-lithotomy position are generally well tolerated in the office. However, in the geriatric population, the prevalence of joint disorders and prosthetics needs to be taken into account. For instance, it is estimated that patients aged >65 years are 3.5–4.5 times more likely to undergo total hip arthroplasty than patients <65 years [1]. Foam or gel padding of the ankles, calves, and knees are advocated to release pressure on these areas. Limited flexibility and range of motion in this population is also a consideration in positioning. Perioperative lower-extremity motor neuropathy resulting from prolonged lithotomy position is of less concern in the office procedure setting given the likely short period time that patients will remain in lithotomy position [2, 3]. Complications of compartment syndrome are also unlikely in the office setting as they tend to occur in the operating room when surgical times exceed 4–6 h [4].

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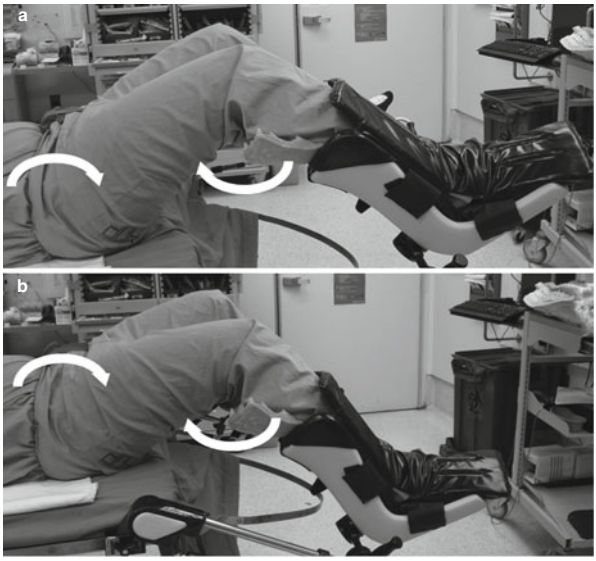

Fig. 3.1 (**a**) Standard lithotomy position. (**b**) Low lithotomy, please note that the hip and knee joints are flexed no more than 90° and pressure points are padded (foam). Curved arrows show that the knee and hip joints are flexed no more than 90 degrees.

Catheterization

Catheterization may be needed in several scenarios in the office setting. Non-indwelling or straight catheterization may be used to obtain a sterile specimen for urine culture or, to determine post void residual (PVR) urine volume. Alternatively, in the case of urinary retention, an indwelling urinary catheter is generally placed. The insertion and maintenance of indwelling catheters are important for the elderly population and their care-givers. Roughly 5–10 % of all nursing home patients and up to 18 % of nursing home patient with lower urinary tract symptoms (LUTS) have Foley catheters [5, 6]. General catheter care involves maintaining a closed drainage system to avoid ascending infection, regular daily cleaning of the area that exits the genitalia to prevent encrustation and irritation, and most importantly, removal of the indwelling catheter at the earliest possible time point [7]. Long term indwelling catheterization comes with many potential complications including recurrent infections, blockage, leakage, urethral erosion, and loss of cyclical bladder function [7, 8]. In patients who are unable to void spontaneously, clean intermittent catheterization is preferred to chronic indwelling catheter. If patients are unable to perform intermittent catheterization, suprapubic tube drainage is an alternative option but comes with the increased morbidity associated with establishing the suprapubic drainage tract. Suprapubic drainage can limit some complications of having long-term transurethral indwelling catheter drainage such as urethral erosion but have not been found to decrease catheter associated bacteriuria [9].

Sterile technique including sterile gloves, cleansing of the urethra and surrounding genitalia, and use of a sterile catheter is recommended in the office or hospital setting. Self-intermittent catheterization does not require sterile technique, but hand washing and avoidance of gross contamination is recommended. Liberal use of lubricating jelly or 2 % lidocaine jelly will aid the ease in passage of the catheter. Visualization of the urethral meatus in postmenopausal female patients may be limited secondary to intravaginal retraction of the urethral meatus. In this situation, gentle placement of a finger in the vagina along the anterior vaginal wall to palpate the urethral meatus can help to guide catheter placement [10].

There are several potential obstructions to the smooth placement of a transurethral catheter including severe phimosis, prostatic enlargement, false urethral passage, bladder neck contracture, or urethral stricture. In these scenarios a coude catheter, a guide wire with council tip catheter, or filiforms and followers may be needed (Fig. 3.2). Ultimately, if a patient is experiencing urinary retention and a practitioner is unable to pass a transurethral catheter, flexible cystoscopy to directly visualize the urethral lumen and level of obstruction or suprapubic tube placement may be necessary. In the office setting, a urologist should have a variety of instruments and tools readily available to in order to troubleshoot difficult catheterization issues.

Urethral Dilation

In the setting of urethral stricture or meatal stenosis urethral dilation may be necessary. A local anesthetic of 2 % lidocaine jelly can be administered transurethrally prior to instrumentation [11]. It is critical that the lumen of the stricture be intubated properly to avoid creation of a false passage. The safest method is to use cystoscopy for direct visualization of the urethral lumen and then pass a wire through the cystoscope and the narrowed lumen into the bladder. Over the wire sequential dilators are generally passed until an appropriate luminal diameter is achieved (Fig. 3.3). Following dilation the physician may place a temporary indwelling transurethral catheter for stenting, recommended intermittent self-catheterization, or simply have the patient return to the office at a designated time point for interval evaluation.

Cystoscopy

Cystoscopy, or cystourethroscopy, is a procedure that allows visualization of the urethra and entire bladder. This can be performed in the office with or without local anesthesia (2 % lidocaine jelly or intravesicle lidocaine). The use of intraurethral lidocaine jelly largely remains individual practice preference. Limited data has indicated that intraurethral injection of lidocaine jelly prior to rigid cystoscopy in male patients helps to decrease pain associated with the procedure [11]. Cystoscopy can

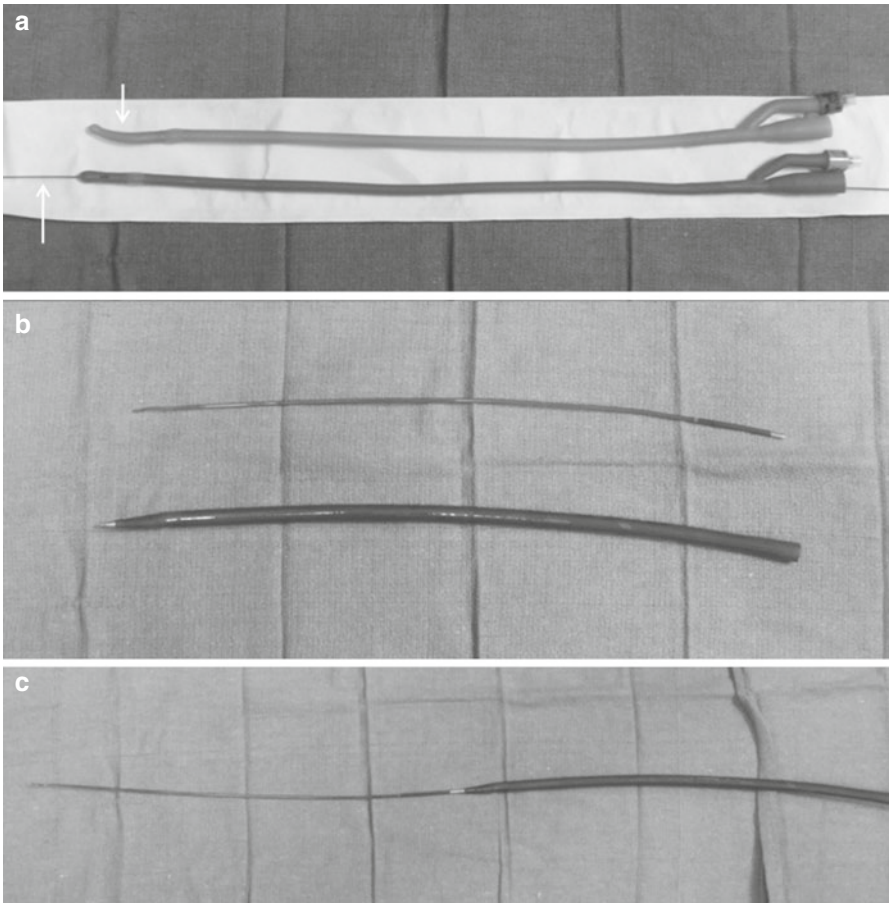

Fig. 3.2 (**a**) Coude catheter on *top, arrow* highlights curved tip that allows this catheter to pass through an enlarged prostate, council catheter on *bottom, arrow* highlights ability of this catheter to be passed over a wire. (**b**) Filiform on *top,* this instrument is soft and pliable that allows it to traverse a stricture, follower on *bottom*, this instrument is the dilating element. (**c**) Filiform and follower connected

be performed using a rigid or flexible cystoscope (Fig. 3.4). Flexible cystoscopy may be performed in the supine position in males and the "frog-legged" position in females, but rigid cystoscopy requires the patient to be placed in lithotomy position regardless of gender. For the comfort of the patient, the smallest diameter cystoscope should be used during rigid cystoscopy (generally 17 French). During cystoscopy, a sterile fluid, generally normal saline is used to distend the urethra and bladder and aid in visualization. Biopsies can be obtained by passing forceps through the working channel of the cystoscope. Fulguration of biopsy sites or other areas of the bladder can be performed using Bugbee electrocautery, however glycine, sorbitol or water must be used as the irrigant if monopolar electrocautery is

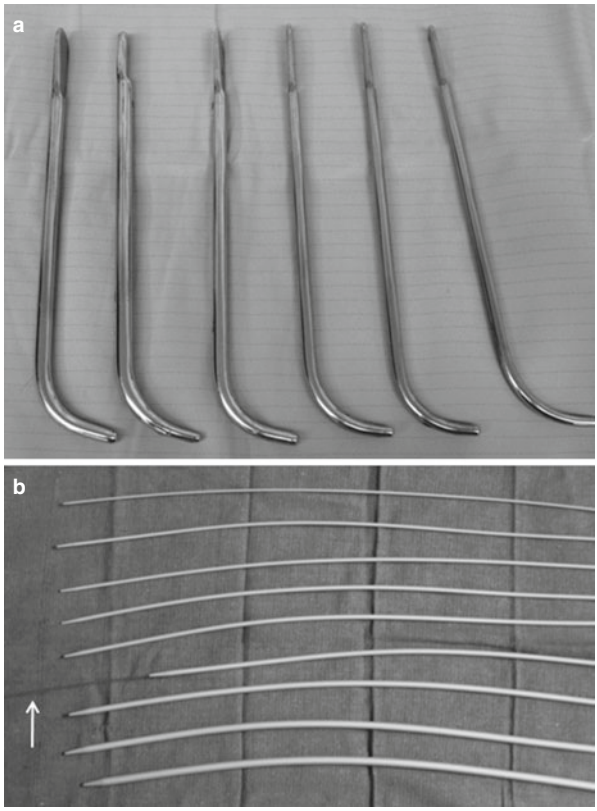

Fig. 3.3 (**a**) Serial sound dilators. (**b**) Serial urethral dilators, *arrow* highlights ability of these dilators to be passed over a wire

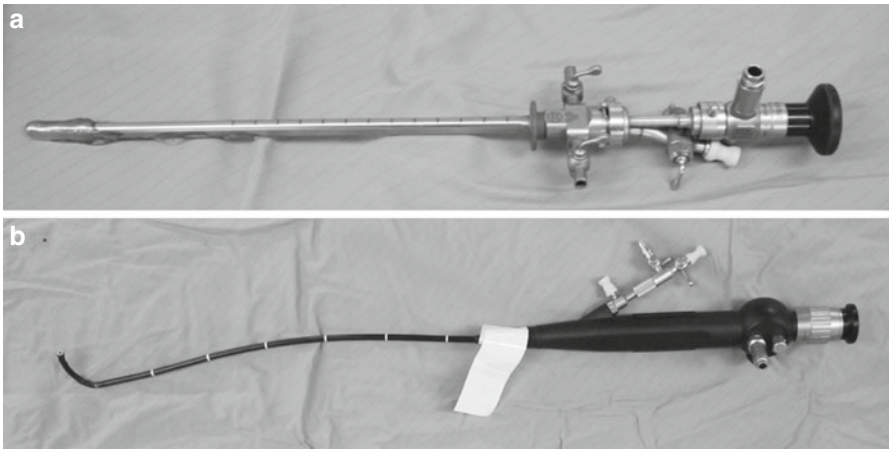

Fig. 3.4 (**a**) Rigid cystoscope. (**b**) Flexible cystoscope

going to be used. Laser ablation of bladder tumors, lesions or stones can be performed using various wavelengths of laser energy and specific laser fibers. Prior to performing bladder biopsy or any further instrumentation beyond basic cystourethroscopy in the office setting, the patient's level of comfort must be assessed and antibiotics are generally given. If necessary, further instrumentation can be postponed and performed in the operating room in order for a patient to tolerate the procedure.

Reasonable effort should be made to ensure the patient has sterile urine before proceeding with any urological instrumentation. Current American Urologic Association (AUA) guidelines state that in cystography, simple cystourethroscopy, urodynamic studies, and removal of an external urinary catheter, antibiotic prophylaxis is not required or recommended. However, prophylaxis is indicated in patients with certain risk factors that affect host-response to surgical infections, which includes but is not limited to advanced age, poor nutritional status, and prolonged hospitalzation [12]. The exact definition of "advanced age" is not provided in the AUA guideline but is left to practitioner judgment. There is a greater prevalence of poor nutritional status among the geriatric population with the prevalence of protein-energy malnutrition (PEM) increasing with age. The prevalence of PEM in elderly persons living at home is 5–30 %, in elderly persons living in institutional care is 16–70 %, and in hospitalized elderly persons is 20–60 % [13]. The geriatric population also has a higher prevalence of prolonged hospitalization than similar younger cohorts.

In patients with total joint replacements, prophylaxis is recommended in those who have been implanted within the last 2 years and those patients who are at increased risk of hematogenous total joint infection or bacteremia associated with urologic procedures [12]. Prophylaxis is not needed in patients with plates, pins, or screws. Currently, the American Heart Association (AHA) does not recommend antibiotic prophylaxis for patients undergoing urologic procedures for the prevention of infectious endocarditis [14]. Discontinuation of blood thinning agent is not needed in all situations but the physician should be made aware of any blood thinning medications (aspirin, nonsteroidal anti-inflammatory drugs, warfarin, antiplatelet agents, etc.). If additional treatment beyond basic cystourethroscopy is anticipated, a discussion between the urologist and the patient's primary care doctor should occur in order to weigh risks and benefits of holding blood thinning medications perioperatively. Sulfamethoxazole-trimethoprim and fluoroquinolones can lead to supratherapeutic INR levels in patients taking coumadin [15]. If these antibiotics are given after cystoscopy, appropriate communication with primary care doctors and geriatric practitioners is needed for INR monitoring in elderly patients taking coumadin. In general, antibiotic administration in the geriatric population, where polypharmacy is common, requires careful assessment of the patient's home medications in order to limit medication cross-reactivity and adverse events.

Side effects of cystoscopy are generally mild. They may include dysuria, hematuria, difficulty urinating, and rarely urinary tract infection. Complications are rare but may include stricture formation, acute urinary retention, bleeding, and clot retention.

Botulinum Toxin A Intradetrusor Injections

Botulinum toxin (BTX) is a neurotoxin produced by gram-positive anaerobic bacterium *Clostridium botulinum*. BTX acts at the neuromuscular junction by inhibiting acetylcholine neurotransmitter release resulting in striated muscle relaxation. It has also been found to inhibit the release of neurotransmitter adenosine triphosphate and neuropeptides such as substance P and to down-regulate the expression of purigenic and capsaicin receptors on afferent neurons within the bladder [16]. It is through these mechanisms that BTX is believes to work to treat detrusor overactivity and overactive bladder by both sensory and motor pathways [17]. Serotype A of botulinum toxin is the form most commonly used for treatment of lower urinary tract dysfunction.

Intradetrusor botox injection can be performed in the office with intravesical and/or intraurethral local analgesia and is generally a well-tolerated procedure. Alternatively, patients who are unable to tolerate this procedure of patients with neurogenic bladder dysfunction who are prone to autonimic dysreflexia can have intradetrusor botox injection performed as outpaitient procedure in the operating theatre using IV sedation with careful monitoring throughout the procedure. Prior to injection, patients should have a negative urine culture and should receive perioperative antibiotics. Intradetrusor injection is performed with a rigid or flexible cystoscope by directly visualizing injection of botox in a template of 20–30 injections 2 mm deep and approximately 1 cm apart throughout the bladder. Traditionally, the trigone and dome were avoided [18] however some practioiners advocate for trigonal injections based on the density of sensory nerves in this area of the bladder [19]. Patients undergoing intradetrusor botox injection should be counseled on the possibility of urinary retention and should be willing to perform self-catheterization if necessary. Intradetrusor botox injection is currently recommended by the AUA/SUFU guidelines as a third-line treatment for patients with overactive bladder who have failed first-line behavioral modifications and second-line oral anti-muscarinic therapy [20].

Suprapubic Tube Placement

The placement of a suprapubic tubes (SPT) is often employed in urology for patients with neurogenic bladder (who cannot perform intermittent straight catheterization) or when urethral access to the bladder is not feasible (trauma, severe stricture disease). Two recent large studies of 219 and 549 patients each, found that the average age at time of SPT placement was 73 years and 66 years of age, respectively [21, 22]. As such, it is important that elderly patients, their families, and primary caregivers be aware of long-term common complications of SPTs such as urinary tract infections and catheter blockages.

Placement of a suprapubic tube is best performed in the operating room in a controlled setting either through an open incision or percutaneously (with or without the aid of cystoscopy and/or ultrasound). Placement of an SPT in the office should be reserved for emergency situations and should be aided by cystoscopy if feasible as serious complications such as bowel injury, vascular injury, and SPT misplacement can occur.

When performed in the office, the bladder should first be fully distended and the patient placed in trendelenburg to shift the intestines cephalad. After local anesthesia is given, a small transverse skin incision should be made about 3–4 cm (or two finger-breaths) above the pubis. Next, a long spinal or "finder" needle should be placed in midline perpendicular to the skin and not too cephalad (away from the bladder) or too caudad (too close to the bladder neck). Urine should be aspirated from the spinal needle to confirm placement if a cystoscope is not already in the bladder to confirm placement. Next, either a Rousch trocar or cystotomy catheter kit may be inserted in the same direction and aside the spinal needle. For the Rousch trocar, a catheter is placed through the hollow lumen, which is then "peeled" away (Fig. 3.5). For the cystotomy catheter kit, the obturator is removed leaving the catheter in place (Fig. 3.5).

SPT care is similar to an indwelling urethral catheter (See above). Most urologist exchange SPTs every month in the office, however if encrustation and occlusion are a problem, then exchange may be needed every 2–3 weeks.

Patients that have long term indwelling transurethral or suprapubic catheters are at increased risk of developing bladder cancer and should undergo routine cystoscopic surveillance. A historical cohort study in the spinal cord injury population showed that patients using solely indwelling catheters had a significantly greater risk of bladder cancer (relative risk [RR] = 4.9; 95 % CI, 1.3–13.8) than those using nonindwelling methods [23].

Urodynamics

Urodynamics are an important aspect of any urologic practice. Elderly patients may be referred for urodynamics for a variety of reason including bladder outlet obstruction, pelvic organ prolapse, overactive bladder, and urinary incontinence. Of all these reasons, urinary incontinence is perhaps the most bothersome to elderly patients and their caregivers. In fact, incontinence affects as many as 40 % of patients in nursing homes and accounts for a significant amount of urodynamic referrals in this population. This section will define the urodynamic evaluation as standardized by the International Continence Society (ICS) [24], and will discuss when relevant specific application to the elderly population.

Non-invasive uroflowmetry is the simplest methodology in urodynamics. It should be noted, that this method is largely dependent on voided volume (minimum of 150 cc required) and a normal maximum flow rate is derived from nomograms based on age and sex. In men, the lowest acceptable maximum flow rates are

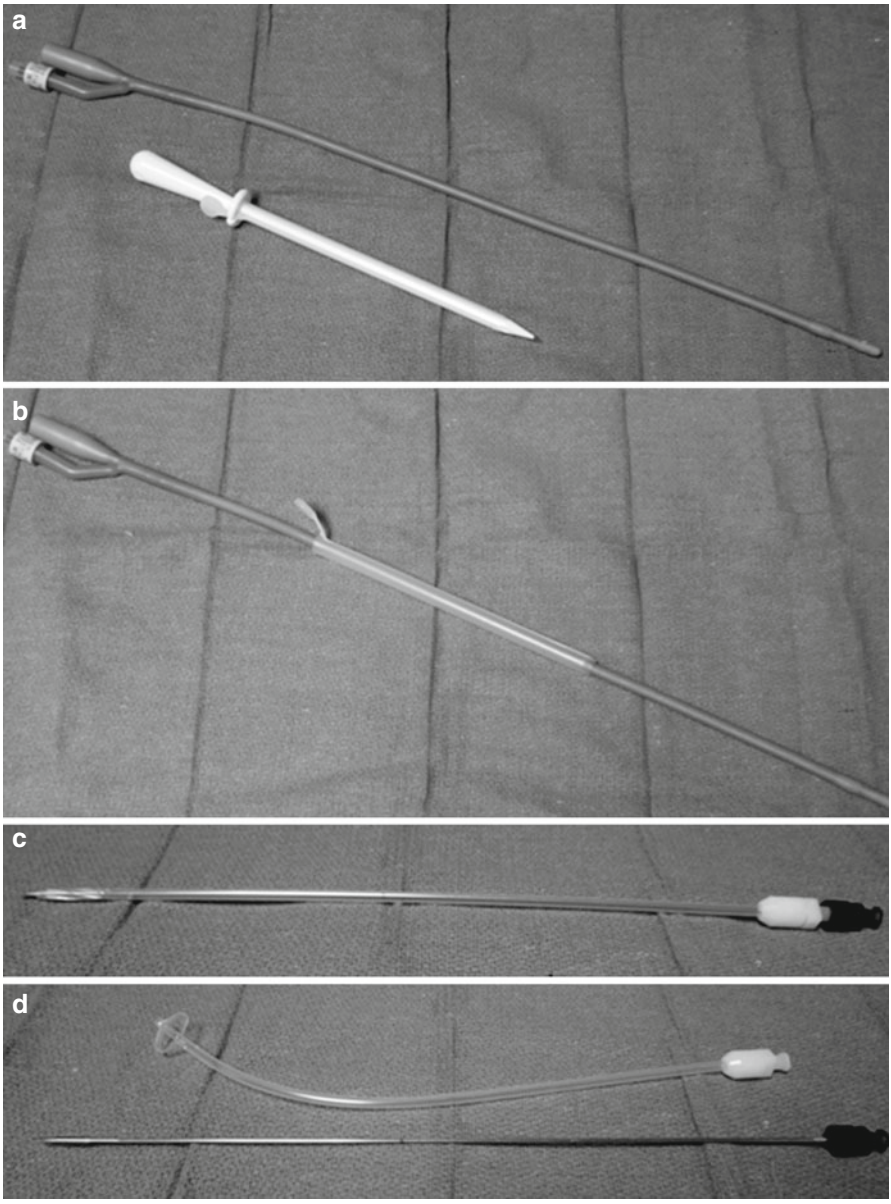

Fig. 3.5 (**a**, **b**) Rousch trocar. (**c**, **d**) Cystotomy catheter kit with self retaining head

21 ml/s, 12 ml/s, and 9 ml/s in age groups of 14–45 years, 46–65 years, and 66–80 years respectively. In women maximum flow rates should be greater than 18ml/s, 15 ml/s, and 10 ml/s in age groups of 14–45 years, 46–65 years, and 66–80 years respectively [25]. In general, most people would accept >15 ml/s as normal [26].

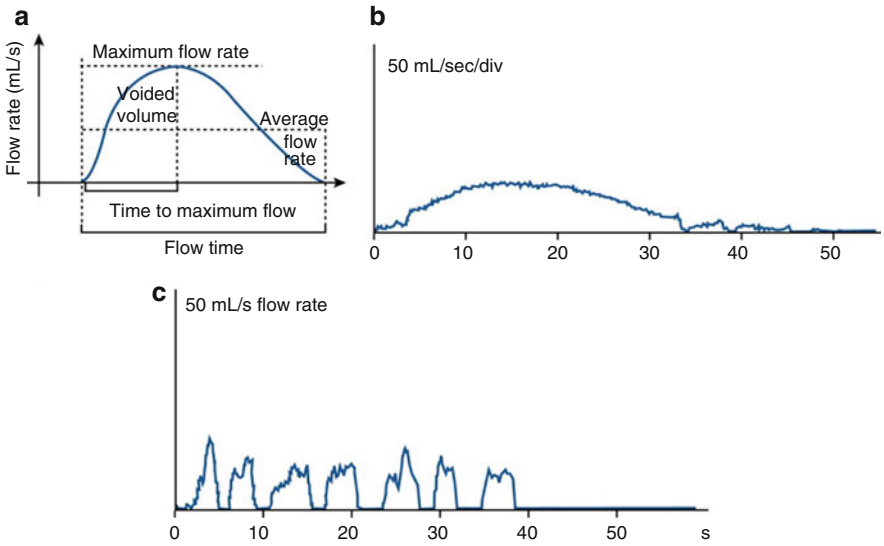

Fig. 3.6 (**a**) Ideal uroflowmetry curve. (**b**) Obstructed voiding pattern on uroflometry. (**c**) Straining voiding pattern on uroflometry (Printed with permission from Elsevier)

Table 3.1 Uroflowmetry

Term (units)	Definition
Urine flow	1. Voluntary urethral passage of urine described in terms of flow rate and flow pattern 2. Flow pattern may be either continuous (no interruption) or Intermittent (interruptions present)
Flow rate (ml/s)	Volume of urine expelled via the urethra per unit time
Voided volume (ml)	Total amount of urine expelled via the urethra
Maximum urine flow rate (ml/s)-Qmax	Maximum measured value of the flow rate correcting for artifact
Flow time (sec)	The time over which measurable flow actually occurs
Average urine flow rate (ml/s)-Qave	Voided volume divided by the flow time
Voiding time (sec)	Duration of the void including interruptions, voiding time equals flow time when voiding is completed without interruptions
Time to Maximum flow (sec)	Elapsed time from the onset of urine flow to maximum urine flow

Figure 3.6 represents the ideal uroflowmetry curve and examples of uroflometry for an obstructive and straining voiding pattern [27]. Table 3.1 defines the terminology [24]. In combination with uroflowmetry, post void residual urine measurement (PVR) urine completes the non-invasive urodynamic evaluation. PVR measurements are typically assessed by ultrasound exam (or catheterization) immediately after voiding Any further delay in PVR measurements risks a false elevation in the

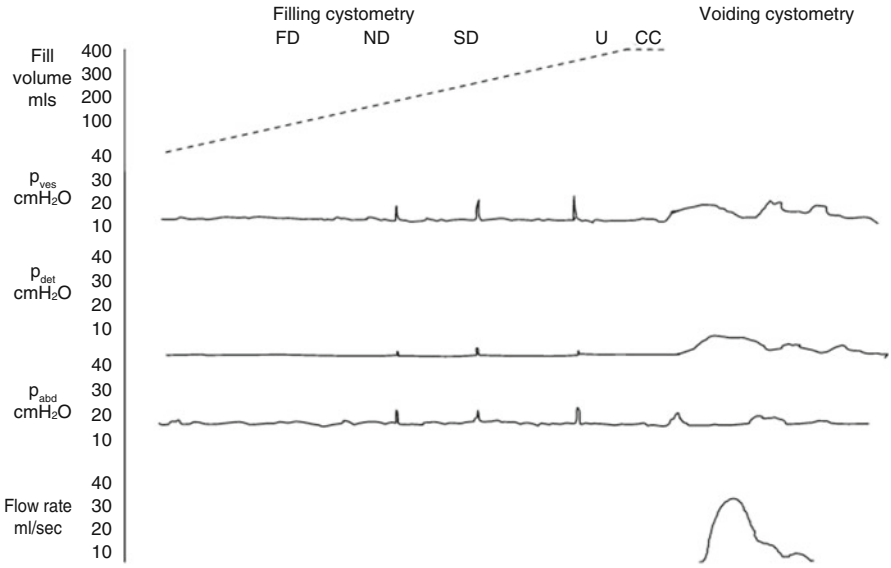

Fig. 3.7 Normal cystometrogram, please note normal compliance and no detrusor overactivity (Printed with permission from Springer)

value from continued urine production. The definition of an elevated PVR is not standardized and remains widely variable between physicians and clinical situations. In general, a value of greater than 150 mL is generally accepted as elevated however patients may remain asymptomatic with PVRs greater than 300 mL or may be symptomatic with PVRs less than 150 mL [28].

Cystometry refers to the measurement of the pressure/volume relationship of the bladder during filling and voiding. Cystometrogram is the graphical recording of the bladder pressures and volume over time during the filling phase, which commences when filling starts and concludes when the patient is given permission to void (Fig. 3.7) [24].

The goals of filling cystometry are to assess bladder sensation, bladder capacity, detrusor overactivity, and bladder compliance. Bladder filling during UDS may be performed at a physiologic rate or non-physiologic (i.e., greater than the predicted maximum rate of urine production). Common filling rates used in practice are 10–100 ml per minute with most practitioners using 50–75 ml per minute. Bladder sensation is assessed by questioning the patient about what they feel in their bladder. These parameters are detailed in Table 3.2 [24]. Pain during filling is abnormal and should be noted by the clinician.

Bladder capacity may be assessed in several ways. The first is the functional bladder capacity, which is the largest voiding volume recorded in a voiding diary [29]. Second, cystometric capacity is the bladder volume when the patient is given permission to void during cystometric testing. Finally, maximum cystometric

Table 3.2 Clinical parameters for bladder sensation

Term	Definition
First sensation of bladder filling	Sensation when the patient first becomes aware of bladder filling.
First desire to void	First feeling that the patient may wish to pass urine.
Normal desire to void	The feeling that leads the patient to pass urine at the next convenient moment, but voiding can be delayed.
Strong desire to void	The persistent desire to pass urine without the fear of leakage
Urgency	Sudden, compelling desire to pass urine which is difficult to defer.
Bladder oversensitivity	Increased perceived bladder sensation during bladder filling with (1) an early first desire to void (2) an early strong desire to void, which occurs at low bladder volumes (3) low cystometric bladder capacity (4) no abnormal increase in detrusor pressure
Reduced bladder sensation	Bladder sensation is perceived to be diminished during filling cystometry
Absent bladder sensation	The patient reports no bladder sensation during filling cystometry

Table 3.3 Detrusor overactivity terminology

Term	Definition
Phasic detrusor overactivity	Characteristic wave form and may or may not lead to urinary incontinence
Terminal detrusor overactivity	Single, involuntary detrusor contraction occurring at cystometric capacity which cannot be suppressed and results in incontinence usually with bladder emptying.
Idiopathic detrusor overactivity	When no defined cause for detrusor overactivity (replaces detrusor instability)
Neurogenic detrusor overactivity	When there is a relevant neurological condition in the setting of detrusor overactivity

capacity is the bladder volume when the patient can no longer delay micturition during cystometric testing [24].

Normal detrusor function during filling cystometry is defined as little or no change in detrusor pressure with filling. In addition, there should not be any involuntary bladder contractions.. Detrusor overactivity refers to the involuntary contractions during filling that may be spontaneous or provoked producing a waveform of variable duration and amplitude. Relevant terminology to detrusor overactivity is listed in Table 3.3 [24].

The final component of filling cystometry is compliance. Compliance is defined as the change in bladder volume divided by the change in detrusor pressure during the change in bladder volume and it is expressed as ml per cm H_2O. The ICS recommends two distinct points on the CMG to calculate compliance: (1) Starting point for compliance is the detrusor pressure at the start of bladder filling and the corresponding volume (usually zero) (2) End point for compliance is the detrusor pressure and bladder volume at cystometric capacity (or immediately before the start of

any detrusor contraction that causes significant leakage). Abnormally low compliance (<12.5 ml/cm H_2O) is a risk factor for renal deterioration caused by elevated bladder storage pressures transmitting pressure to the upper urinary tract.

Lastly, leakage of urine during filling cystometry should also be assessed for and described in detail. Urodynamic stress incontinence is the involuntary leakage of urine during filling cystometry and is associated with increased intra-abdominal pressures in the absence of a detrusor contraction.

Abdominal leak point pressure (ALPP) is a dynamic pressure induced by an increase in abdominal pressure (cough or valsalva) and is measured at the lowest value of increased intravesical pressure that provokes urinary leakage in the absence of a detrusor contraction. It is assessed at a fixed bladder volume (at least 150–200 ml) and is used as an objective measure of stress urinary incontinence in women [29]. Typically ALPP of less than 60 cm H_2O indicates intrinsic sphincter deficiency (ISD), a value of 60–90 cm H_2O suggests a combination of ISD and urethral hypermobility, and a value of greater 90 cm H_2O suggests primarily urethral hypermobility [30]. Detrusor leak point pressure (DLPP) is a static pressure measured as the lowest value of the detrusor pressure at which leakage is observed in the absence of increased abdominal pressure or a detrusor contraction. This is only seen in patients with neurogenic bladder dysfunction and generally seen in patients with poor bladder compliance. In these instances, urethral leakage is essentially a "pop-off" mechanism to relieve the rise in pressure. This pressure measurement reflects the pressure that is transmitted to the upper urinary tract. McGuire first described DLPP in a pediatric population of patients with myelodysplasia [31]. In this setting, patients with a DLPP greater than 40 cm of H_2O were at significantly higher risk of upper tract deterioration than those with pressures less than 40 cm of H_2O.

A pressure flow study is the graphical recording of the pressure volume relationship of the bladder during emptying, which begins when the patient is given permission to void and ends when the patient considers their voiding has finished. A pressure flow study is depicted in Fig. 3.8 [24] and its terminology is described in Table 3.4 [24].

As defined by the ICS, normal voiding is achieved first by voluntary relaxation of the urinary sphincter (i.e., reduction in intra-urethral pressure) followed by a continuous detrusor contraction leading to complete bladder emptying within a normal time span [24]. Conversely, detrusor underactivity (DU) is defined as a contraction of reduced strength and/or duration resulting in prolonged bladder emptying and/or a failure to achieve complete bladder emptying within a normal time span in the absence of obstruction.

DU is a clinical syndrome that can be due to many causes such as fecal impaction, diabetes, medication, and impaired mobility [5]. It has been shown that detrusor function declines with age and is under-diagnosed in the geriatric population as a cause of LUTS. Impaired detrusor contractility (IDC) is used to describe this functional loss in detrusor strength. Urodynamic studies in elderly institutionalized patients with urinary incontinence revealed that overall 61 % suffer from uninhibited detrusor contractions and that half of these patients also have IDC [32]. This

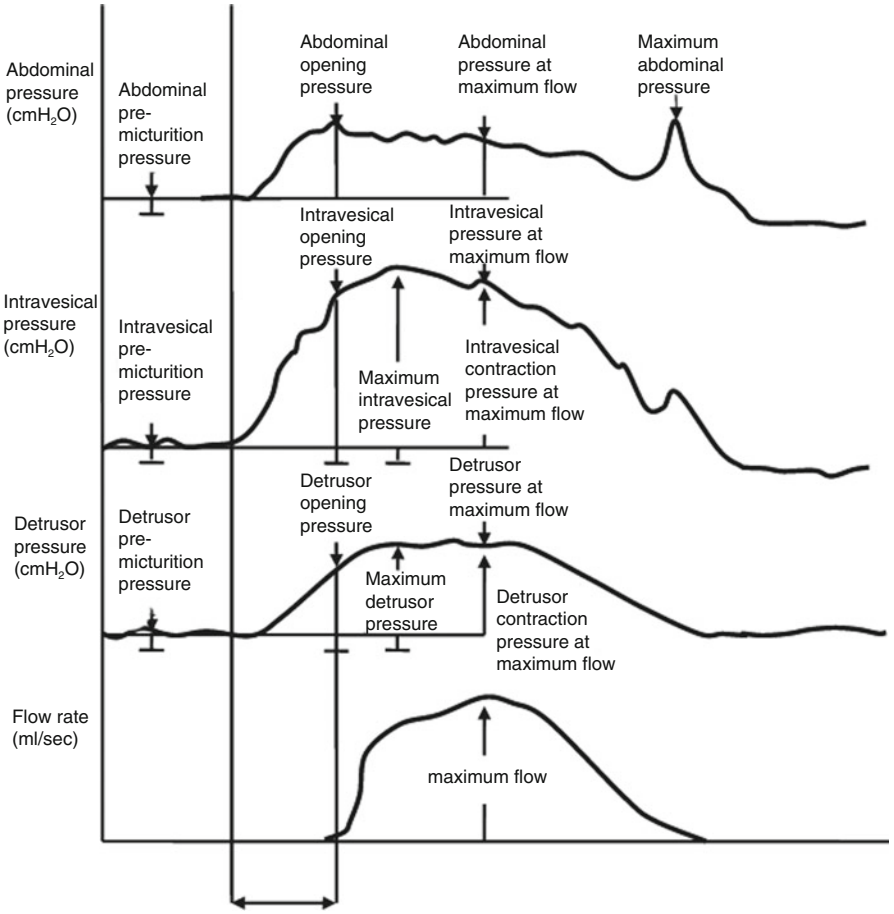

Fig. 3.8 Pressure flow study (Printed with permission from Springer)

entity of DU with IDC and involuntary contractions is known as detrusor hyperactivity impaired contractility (DHIC). More recent data has shown that DU with IDC is present in 48 % of elderly men and 12 % of elderly women in the community presenting with LUTS. Furthermore, two thirds of these men and one half of these women had concomitant DHIC [6]. These results underscore the importance of recognizing DHIC during office urodynamics.

Lastly, video urodynamics utilizes fluoroscopy to visualize the lower urinary tract during filling cystometry and pressure flow urodynamics. It may be utilized when assessing for a specific site of obstruction (bladder neck dysfunction), unexplained retention in women, pelvic organ prolapse, neurogenic voiding dysfunction, and complex incontinence. Clearly many of these clinical situations are present in the elderly patient with lower urinary tract symptoms.

Table 3.4 Pressure flow

Term	Definition
Premicturition pressure	Pressure recorded immediately before the initial isovolumetric contraction
Opening time	Time elapsed from initial rise in pressure to the onset of flow and reflects the time taken for fluid to pass from the point of pressure measurement to the uroflow transducer
Opening pressure	The pressure recorded at the onset of measured flow
Maximum pressure	Maximum value of the measured pressure
Pressure at maximum flow	Pressure recorded at the end of measured flow
Contraction pressure at maximum flow	Difference between the pressure at maximum flow and the premicturition pressure
Flow delay	Delay in time between a change in pressure and the corresponding change in measure flow rate

Peripheral Tibial Nerve Stimulation

Peripheral tibial nerve stimulation (PTNS) is recommended as a third line treatment for patients with overactive bladder by the 2014 AUA/SUFU guideline [20]. Most studies report improvement in incontinence, frequency, nocturia, and quality of life. Peters et al. conducted a study comparing a PTNS group to a sham-PTNS group that revealed only the active treatment group showed improvements in frequency, nocturia, and urgency incontinence [33]. Reported adverse events were uncommon and very mild including ankle bruising, discomfort at the needle site, bleeding at the needle site, and leg tingling [33]. PTNS can be administered in an office-based setting as 30 min of stimulation weekly for 12 weeks usuing a 32 guage needle.

PTNS may be a good option for elderly patients with overactive bladder who have failed behavioral modifications and oral therapies. A study by Zinkgraf et al. showed that PTNS improves urinary frequency, incontinence, and urinary retention specifically in an elderly population [34]. For patients who require third-line modalities, PTNS offers a minimally invasive treatment option with relatively few side effects compared to intradetrusor botox injection or sacral neuromodulation. PTNS can be performed in an office-based setting and without the need for anesthesia, additional medications and antibiotics, or withholding blood thinning medications.

Conclusions

This chapter set out to describe basic urologic office procedures and how these must be adapted to meet the needs of the elderly population. Specific attention must to be paid to patient positioning. Furthermore, urologic practitioners should be updated on indications for antibiotic prophylaxis as total joint replacements and valvular

heart diseases are not uncommon in the elderly. When antibiotics or new medications are prescribed, it is important to consider potential drug interactions and polypharmacy for the elderly population. Patients and caregivers must also be educated on proper care of indwelling catheters as these are often used to manage the lower urinary tract of the geriatric population. Finally, urologists must also be aware of changes in the lower urinary tract with age and be able to adjust for this when performing non-invasive urodynamics (uroflow and PVR) and be able to recognize DHIC on cystometry and pressure flow studies. This level of alertness to the urologic care of the elderly will ultimately benefit not only patients but also their caregivers and families.

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Chapter 4
Medication Issues

Mary Ann Forciea

Case Presentation

Mrs. L is an 82-year-old retired university professor who presents for the evaluation of urinary incontinence of 3 years duration. She leaks urine daily, and wears "maxi pads" daily. She does experience increased leakage while playing tennis, and did note worsening during a recent upper respiratory infection. She is functionally independent, lives alone, and plays tennis weekly. Her active medical problems include hypertension, diabetes mellitus, hyperlipidemia, glaucoma, and osteoarthritis of the lumbosacral spine. Her current daily medications include: aspirin, hydrochlorthiazide, metoprolol, enalapril, metformin, simvastatin, naproxen, and pilocarpine eye drops. She asks if anything can be done to improve her continence.

General Review of Medication Issues in Older Patients

The burden of medication management is especially important in the care of older patients since they carry a disproportionate share of chronic conditions and drug therapy: while approximately 13 % of the population of the US is >65 years of age, these patients purchase 33 % of all prescription drugs [1]. Increasingly, conditions such as congestive heart failure and diabetes are managed with small dose of medications from a variety of classes. The potential for adverse drug events and problems with patient adherence increase as the medication burden increases. Increasingly, medication choices are included in performance management measures [2].

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Optimal medication management for patients of any age follows the adage,

The correct *drug*
In the correct *dose*
For the correct *patient*
At an affordable *cost*

Treatment of older patients can require special considerations at each of these steps.

The "Correct" Drug and Dose

1. *Pharmacokinetic* considerations with age: "Start low, go slow."

   The time course of action of a drug and its metabolites constitute its *pharmacokinetic* properties. These properties of drugs are usually grouped into changes in their *absorption*, *distribution*, *metabolism*, and *elimination*. Considerations in each of these four areas can be important in older patients.

   (a) *Absorption*

   In general, few clinically significant changes in drug absorption from the GI tract are seen in older patients. More important can be drug administration factors which can influence absorption:

   – Decreased gastric pH (either intrinsic or due to acid secretion blockers) may change absorption of antibiotics or vitamins
   – Alterations in GI motility due to constipation, diarrhea, or medications may change absorption due to transit time alterations through various segments of bowel
   – Simultaneous administration of medications can create obstacles to absorption: medications like calcium may adsorb other medications such as synthroid or fluoroquinolone antibiotics
   – Parenteral tube administration of medications can be complicated by interactions with feeding solutions or by changes in motility related to osmolality changes in the feeding solutions

   Cooperation among care teams especially in inpatient and nursing home settings is essential to design medication administration schedules which maximize absorption of needed medications. Consultant long-term care pharmacists can be of great assistance in this endeavor.

   (b) *Distribution*

   Drug distribution is usually expressed as a volume of distribution (V_d) with units of volume or volume per weight. Drug penetration into the body spaces and time to steady state concentration alters with aging due to age-associated body composition changes. Body fat content increases, so that lipophylic drugs have a larger volume of distribution. Drugs such as flurazepam take longer to reach steady state and require longer times for elimination.

In addition, transport factors can influence distribution. Albumin, the plasma protein most associated with drug binding, can be reduced in concentration in older patients. Reduced protein binding may result in elevated-free levels, and potentially increased toxicity. Two drugs influenced by this phenomenon are warfarin and phenytoin.

(c) *Metabolism*

The liver and kidneys are the two organs most associated with drug metabolism in older patients.

Liver metabolism of drugs in older patients can be reduced because of decreased hepatic blood flow and by decreased hepatic mass. In the liver, drugs are metabolized by phase I or phase II pathways. Phase I reactions include hydroxylation, oxidation, dealkylation, and reduction. Metabolites can be equipotent, less potent or more potent than the original drugs; effects can be unpredictable in older patients. Phase II reactions involve glucuronidation, conjugation, or acetylation. These metabolites are generally inactive and are less likely to contribute to toxicity.

The kidneys are actively involved in Vitamin D metabolism, converting 25-hydroxy Vitamin D to the highly active 1, 25, dihydroxy Vit D. Declines in kidney function can contribute to vit D deficiency syndromes in patients with renal failure.

(d) *Elimination*

Terms useful in consideration of the elimination of drugs from the body are:

Clearance—the volume of plasma or serum from which a drug is removed per unit of time, L/min

Half-life—time required for a drug concentration to decline by 50 %

Steady state—the amount of drug entering the circulation equals the amount eliminated. Most drugs reach steady state concentration after five half lives

While liver alterations may play a role in the elimination of some drugs, most drugs and metabolites require renal involvement for elimination. While renal tubular excretion can change with aging, most attention has focused on the declines in glomerular filtration with aging. Declines in glomerular filtration can vary with individuals, and are poorly reflected in the serum creatinine. The traditional algorithm for calculating GFR (via creatinine clearance-CrCl) is the Cockcroft–Gault equation [1]:

$$\text{Creatinine Clearance} = \left\{(140 - \text{age}) \times \text{weight}(\text{kg})\right\} / (72 \times \text{serum Cr}).$$

The value of the equation is usually reduced to 85 % in women. While many electronic medical record systems report Cr Cl via the Cockcroft–Gault equation, the clinician must remember that the equation become less reliable in situations of low flow and low muscle mass which are commonly seen in older frail patients. *Whenever possible*, *measurement of blood levels of drugs* (*aminoglycosides*, *anticonvulsants*) *in older patients is the best guide to dosing levels*.

Pharmacodynamics, the time course and intensity of effect can vary widely and unpredictably in older patients. Morphine can produce slightly longer pain relief in some older patients, for example. Adjustments in initial dose and dosing intervals may be required for many medications.

When initiating a new medication in an older patient, the adage "starts low, go slow" remains useful: start with small initial doses, with longer dose intervals; increase dose or alter intervals as symptoms require. Table 4.1 summaries these principles.

The "Correct" Patient

Choosing the *best medication* at the right dose and dosing interval for your individual patient is the foundation of prescribing for patients of any age. In selecting a medication for an older patient, certain factors may influence the choice of an initial medication:

Effectiveness—new drugs are rarely tested in older patients due to age-based elimination from initial drug study panels. While the FDA is encouraging more inclusive criteria in patient selection for initial testing, issues of coexisting disease will likely continue to limit the inclusion of representative older patients in studies. Prescribing a newly licensed drug to older patients requires the ability of the patient and physician to identify and monitor both effectiveness and side effects in this population. Often, the choice of an established medication is safer for an older patient.

Harms

- Adverse effects of newly licensed medications are unpredictable in older patients
- Certain classes of medications are more likely to cause an adverse effect in an older patient
  - Anticholinergic drugs may precipitate acute glaucoma, bladder outlet obstruction, bradycardias, and syncope. Donepezil prescribed for memory loss is increasingly reported as linked to bradyarrhythmias and syncope

Table 4.1 Summary of pharmacokinetic changes with aging

	Age-associated change	Medication examples
Absorption	Increased possibility of drug–drug interactions in GI tract (polypharmacy)	Proton pump inhibitors and antibiotics, calcium salts and synthroid
Distribution	Increased body fat stores Decreased albumin concentration and drug binding	Anesthetic agents-warfarin, phenytoin
Metabolism	Decreased liver metabolism	Benzodiazepines
Elimination	Decreased renal clearance	Aminoglycosides, anticonvulsants

- Opioids will increase constipation, and may cause confusion
- Antibiotic use may result in bacterial overgrowth colitis

A commonly used source of medications to be potentially avoided in older adults is the "Beers list" [3, 4]. A sample of drugs appearing on the list with rationale appears in Table 4.2. If an individual patient has a strong preference for a medication on the Beer's list, chart documentation of the rational should be provided.

- Drug–drug interactions are more likely due to the increased average number of medications taken by older patients.

Cost—many older patients are on limited income, and take multiple medications. Most seniors are now using insurance plans with established formularies to help pay for medications; either Medicare "Part D" plans or state Medicaid formularies. Established medications are more likely to be included in these formularies and require less staff time with preauthorization for use.

Adherence: "Affordable Cost" and Other Factors

Older patients may experience special barriers to filling prescriptions and continuing medications as prescribed. Studies have shown that approximately 50 % of older patients have adherence issues with at least one medication. Complicating things further, patients may be non-adherent with one medication and adherent with others [5]!

Cost—Pharmacy data suggests that as many as 40 % of prescriptions are never "picked-up" by patients. Cost is a major factor in this initial loss of adherence, as well as with ongoing care. As mentioned above, older patients are on a fixed income, and use insurance-based formularies for medications payment. Many of these insurance plans require co-payments for medications. With increasing numbers of prescribed medications, the co-payment amounts may become limiting. Prescribing generic forms of medications whenever possible will aid in this aspect of care.

Table 4.2 A sample of potentially inappropriate drugs for the elderly from the Beer's list

Medication class	Example	Rationale
Nonsteroidal anti-inflammatory agents	Naproxen	Renal failure, GI bleeding
Barbiturates	Phenobarbital	Confusion
Benzodiazepines	Chlordiazepoxide, diazepam	Prolonged sedation
Hypnotics	Diphenhydramine, flurazepam	Confusion, prolonged sedation
Muscle relaxants	Cyclobenzaprine, methocarbamol	Anticholinergic effects
Pain relievers	Meperidine, propoxyphene	Confusion, minimal benefit
Antihypertensives	Clonidine	Bradycardia, orthostatic hypotension

Literacy—Standard prescription labels are too small for many older patients to read, and use medical words which are poorly understood. Some of the larger chain store pharmacies have instituted larger print, more legible labeling practices. Physician offices can assist by providing large print medication lists with instructions for patients at the time of visits.

Manual dexterity—"Child proof" bottles can be extremely difficult for older patients to open. This can result in patients removing pills from their original bottles, which can increase medication confusion. Non-childproof bottles can be ordered for older patients, with cautions if young children are in the home. A wide variety of "pill boxes" which are preloaded by family members or nursing personnel are available. Some of these dispensers are automated, and dispense at a fixed time of day with an alert signal for the patient. Inhaled medications should be ordered with a spacer or nebulizer if the patient cannot demonstrate good multi-dose inhaler technique in the office. Some pharmacies will dispense pills in "blister packs" with all the pills for a given time of day grouped together in a plastic blister. The patient or caregiver opens the blister rather than opening several bottles.

Adverse Events of Medications in Older Patients

It has been estimated that 20 % of all Emergency Department visits by older patients are related to adverse effects of medications. In addition to the risks of individual medications mentioned above, and to drug–drug interactions in patients on multiple medications, older patients have additional risks of adverse effects:

- Vision limitations interfere with prescription label reading and pill identification
- Complex medication administration regimen can be difficult to understand or implement
- Lack of understanding about indication for individual medications can lead to errors
- Cognitive impairment which impacts all of the above. Many of these cognitive impairments are mild enough to escape identification on brief medical encounters, but substantial enough to interfere with medication adherence
- In Nursing Home settings, multiple dosing interval schedules ("TID" is not the same as "every 8 h" for instance), may result in multiple medication nursing passes, and increased opportunities for errors

Clearly written prescriptions which include indication for use and the simplest dosing regimen possible will aid with adherence in any setting. Nursing home physicians should work with pharmacy and nursing staff to streamline medication administration wherever possible [6].

On occasion, patients admitted to a hospital or nursing home with hypertension or diabetes develop complications such as hypotension or hypoglycemia within the first 48 h of admission. Consideration of prior adherence issues at home with medications may be in order before new diagnostic work-ups are initiated. Patients

may NOT, in fact, have been taking their medications as ordered. When medications are ordered from record-based lists and administered by nursing staff, overmedication may result. *Patients or caregivers should be politely but firmly questioned about ACTUAL medications and dosing regimen in use at home*.

Transitions of Care Medication Issues

At discharge from the acute care hospital or nursing home, special care should be taken in the ordering and review of discharge medications [2, 7]. Any deviation from admission medications should be carefully explained. In many instances, hospital formulary composition necessitates changes in medication within a class during the admission. Whenever possible, patients should be returned to their original medication (with which they are familiar and likely have a supply at home), or have careful instructions about in-class medication changes. The risk of duplicate medication without these precautions is high. Returning the patient to a preexisting medication list also alleviates the need to check with the patient's drug plan formulary for availability since the patient had been receiving supplies of baseline medications.

For patients experiencing a major change in function, transfer or admission to a long-term care facility may offer a chance for reconsideration of need for medication [4]. Does the patient's current life expectancy justify ongoing medication? Does the medication fit with the patient's current goals of care? Consultation with specialist pharmacy consultants can greatly assist in this process.

Urinary Incontinence (UI): Medical Management Options

Medications for Urinary Incontinence

Most of the medications available for UI address urge incontinence, and have been shown to be effective in older patients. The antimuscarinic agents differ in anticholinergic potency and metabolism. Table 4.3 lists the commonly available choices. Contraindications to the use of antimuscarinic agents in older patients are:

- A history of urinary retention
- Impaired gastric emptying
- Narrow angle glaucoma

Antimuscarinic agents can be safe in older patients if started at the lowest doses and titrated up as needed and with monitoring. Evaluation of post-void residual urine volume should be considered in those patients who develop increased incontinence on this class of medication, reflecting possible overflow incontinence. Long-term use of this class of medication can be associated with xerostomia, leading to

Table 4.3 Medications available for UI in older patients

Antimuscarinic agents
Oxybutinin (as immediate release, extended release, or patch) 2.5 mg twice daily, max 5 mg twice daily
Tolteridine (immediate or extended release) 1 mg twice daily, max 2 mg twice daily, metabolism CYP 3A4
Trospium 20 mg/day
Darifenacin 7.5 mg/day, max 15 mg/day; liver metabolism, CYP3A4
Solifenacin 5 mg/day, max 10 mg/day metabolized in liver, CYP 450:3A4 substrate
Mirabegron 25 mg/day, max 50 mg/day, liver metabolism CYP 450:2D6, 3A4 substrate
Topical estrogen

increased dental caries and tooth loss. An increase in confusion may also be seen after initiation of antimuscarinic agents. This risk of confusion is especially strong in patients who are receiving anticholinergic medications such as donepezil for dementia. Mirabegron is a B3 receptor agonist and has less anticholinergic potential. Little evidence suggests that one member of the class is superior to another in an individual patient. Choice of agent should depend on adverse event profile, drug interactions, dosing regimen, and cost. Failure of one agent should not preclude a trial of another member of the class.

Topical estrogen may be useful in stress incontinence in postmenopausal women due to improvements in vaginal mucous production.

Behavioral Therapy for Urinary Incontinence

Non-pharmacologic alternatives to the treatment of some urologic problems are available and useful for older patients [8, 9].

Urinary Incontinence treatments offer the widest array of behavioral approaches (See also Chap. 7).

Lifestyle modifications Alterations in daily practices may alleviate the symptoms of urinary incontinence in many patients. Simple adjustments, such as the timing of diuretic administration (moving a second dose from 8 to 4 PM) may alleviate nocturia with leaking. Certain foods can be bladder irritants: spicy foods, citrus fruits, and artificial sweeteners. Caffeine is both a diuretic and a smooth muscle irritant. Food diaries can allow individual patients to track dietary exposures and bladder contraction related urinary leakage. Chronic constipation may contribute to urinary incontinence. Smoking can lead to incontinence due to both increased coughing, and to the bladder contractions associated with nicotine exposure. Weight reduction in morbidly obese women has been shown to result in decreased symptoms of urinary incontinence.

Kegel exercises Patients with stress urinary incontinence related to pelvic muscle relaxation can benefit from a program of pelvic muscle exercise. These exercises

were first described by Dr Arnold Kegel in 1948 [10]. Patients (women and post-prostatectomy men) are taught to:

- Identify pelvic floor muscles—usually taught by asking the patient to contract the rectal muscles used to prevent expelling flatus
- Intentionally contract these pelvic floor muscles, and sustain the contraction for from 2 to 5 s. Patients gradually increase the time of the longer contractions to 10 s
- Repeat these brief and more sustained contractions in sets of 10–30 repetitions three times daily. Patients should rotate positions to include lying, seated, and standing postures

Successful Kegel exercise muscle strengthening has been demonstrated to improve urinary incontinence in women and men, is free (after the original instruction), has no drug interactions, and can improve the older patient's sense of empowerment. Strong evidence supports the efficacy of pelvic floor muscle exercise programs for the prevention and treatment of incontinence. Preoperative training in Kegel exercises can reduce post-prostatectomy incontinence.

Bladder training programs a variety of techniques are available which involve voiding at intervals. Presumably, intentional emptying of the bladder before volume-related continence loss will reduce incontinence. Most of these scheduling programs are followed during waking hours only. These techniques include:

- *Scheduled voiding*—Patients are taught (or reminded) to toilet on a fixed schedule (often every 3 h). While convenient for nursing staff in facilities or for caregivers, the fixed intervals may not match individual patient needs
- *Habit training*—after completion of a voiding diary, a schedule of toileting is developed for an individual patient (perhaps 30 min after breakfast, 2 h later, and then 3 h intervals)
- *Prompted voiding*—this technique can be used by caregivers of patients with dementia. After completion of a voiding diary, patients are asked about wetness or dryness at determined intervals. If dry, they are offered toilet opportunities and/or assistance. Positive feedback for dryness is provided
- Bladder *retraining*—for cognitively intact patients who are motivated to decrease incontinence episodes, an adjustable voiding regimen can be developed. Patients are educated about techniques to reduce urge-associated voiding to prolong intervals between voids. These techniques can include distraction and relaxation strategies. As control increases, intervals between voids are increased

Physical rehabilitation techniques Electrical or magnetic stimulation of the bladder has been proposed in the treatment of urinary incontinence. A review of randomized controlled trials of both techniques has showed limited evidence that these techniques improved continence more than sham controls or pelvic floor muscle training. Biofeedback techniques can improve awareness of pelvic floor muscle contractions, and serve as an adjunct to pelvic floor muscle (Kegel) training. In biofeedback, electrodes are placed on the skin or inside the vagina and rectum. Indices of muscle contraction strength and endurance can be used to help design

individualized programs of exercise. The use of weighted vaginal cones can also improve pelvic floor muscle strength. Women are taught the routines of insertion/removal and cleaning between uses. Women insert the lighted cone and retain it for up to 15 min twice daily. As pelvic muscle strength improves, heavier cones are inserted. The cones are highly acceptable to some patients, but not all. While some evidence exists as to the efficacy of cones, little evidence shows them to be superior to Kegel exercises alone.

Case Presentation Return

After checking for a urinary tract infection and counseling about avoidance of caffeine, Mrs. L should be instructed in pelvic floor muscle (Kegel) exercises. If she has difficulty identifying the appropriate muscles, biofeedback could be included in her treatment plan. She might also benefit from bladder retraining to increase the time between voluntary voids. If her symptoms of urinary incontinence persist, she could begin a trial of oxybutinin.

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Chapter 5
Perioperative Care of the Geriatric Urology Patient

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Introduction

Approximately half of all urologic surgeries in the United States are performed in patients 65 years of age or older [1]. It is also estimated that by the year 2030, 20 % of the United States population will be greater than 75 years old [2]. With the increasing elderly population worldwide, the proportion of patients in this age group presenting for surgery on an annual basis will certainly increase. With proper patient selection, careful planning, and optimal perioperative management, surgery can be safely performed in elderly patients with comparable risk to younger individuals [3]. Although there has been significant improvement over the last few decades in surgical technology and anesthesia delivery, the elderly continue to represent a unique and challenging population of surgical patients.

Preoperative Assessment

While chronologic age should never be considered a contraindication to even elective surgery, it is important to recognize that elderly patients are at increased risk for a number of perioperative complications compared to younger patients who undergo similar surgical procedures [4]. The increased risk of complications for the geriatric surgical patient is multi-factorial [5]. Elderly patients are more likely than younger patients to have more co-morbidities, take more medications, and have an impaired

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functional status [5, 6]. Geriatric patients are often able to handle the initial stress of surgery but some may lack the reserve to handle a complication [7], thus leading to worse outcomes [8]. An estimated 20 % of patients older than 80 years of age who undergo noncardiac surgery will experience a postoperative complication, placing them at greater risk of death [9]. Similarly, a retrospective review of the American College of Surgeons National Surgical Quality Improvement Program database revealed that elderly patients undergoing gastrointestinal surgery have significantly higher rates of morbidity and mortality, even when adjusted for preoperative co-morbidities [10].

While a routine history and physical is standard for any patient prior to a surgical procedure, a detailed assessment of co-morbid conditions, medication history, nutritional status, and functional status is essential to minimize the risk of complications for elderly patients. While taking a history, it is important to recognize that elderly patients may be hard of hearing, have poor memory, and may minimize symptoms out of fear of loss of independence [11]. Up to 40 % of outpatients with cognitive impairment may not actually have the diagnosis of dementia documented in their chart [12].

The goal of the preoperative assessment is to evaluate for perioperative risk and to identify problems that can be optimized before surgery. It is during the preoperative assessment that discussion of postoperative care should begin to ensure that an appropriate postoperative discharge plan is in place.

Medical Co-morbidities

Elderly patients typically have more medical conditions than that of younger surgical patients. Common medical problems seen in the elderly include dementia, Chronic Obstructive Pulmonary Disease (COPD), diabetes, coronary artery disease (CAD), congestive heart failure, and hypertension. The presence as well as the severity of these co-morbidities can be a valuable predictor of postoperative outcome for many urological procedures [13–15]. As one might expect, the presence of co-morbid conditions has been shown to be a more useful predictor of perioperative outcomes than chronologic age alone [16].

Medications

A thorough review of current medications is important as 40 % of individuals 65 years or older are on five or more medications [17]. It is not uncommon for elderly patients to have more than one doctor prescribing them medications. Additionally, medications targeting the cardiovascular and central nervous systems are common prescriptions in this age group. Polypharmacy obviously complicates perioperative management and often requires consultation and coordination with other specialists.

Knowledge of an elderly patient's medication history can reduce the potential for drug interactions. Known allergies and any previous adverse reactions should be sought and documented. Any over-the-counter drugs, herbal, or dietary supplements should also be noted. Older patients are more likely to be taking anti-coagulants, aspirin, and nonsteriodal anti-in flammatory drugs which may need to be stopped for many procedures. Although there is no consensus on optimal perioperative management for these medications, the goal is to minimize the window of time which the patient is at increased risk for thrombosis while balancing the increased risk of perioperative bleeding.

Nutritional Status

The detrimental impact of malnourishment is easily underappreciated by surgeons. Although definitions of malnourishment vary between studies, the rate of malnourishment in urology patients is estimated at around 16–21 % [18, 19]. Malnourishment increases with age and can result from multiple factors, including underlying co-morbidities, poor dentition, poor functional status, and medications that alter digestion, absorption, appetite, taste, and smell [20, 21].

Malnourishment is a significant risk factor for postoperative complications following urologic surgery [22]. This is especially true for patients undergoing radical urologic surgeries, where malnourishment may be the strongest risk factor for morbidity and mortality [19, 23]. These findings are consistent with previous literature from Gibbs et al. which showed that low preoperative albumin is the strongest predictor of morbidity and mortality in major noncardiac surgery [24]. However, serum albumin levels do not just reflect an inadequate dietary intake, but may also be affected by co-morbidities, inflammatory cytokines, and medications [18, 25, 26].

Regardless, it is clear that adequate nutrients are required for proper surgical wound healing and recovery from the catabolic stress of surgery [27–30]. Total Parental Nutrition (TPN) has been used, but, offers minimal benefit to surgical patients and increases infectious risk [31, 32]. Interventions such as jejunostomy and gastrostomy feedings have been tried but are highly invasive and not without complications [33]. Early postoperative oral feedings have been shown to shorten length of hospital stay [34], however, it offers little benefit to patients who are malnourished prior to surgery. Preoperative oral nutritional supplementation has been shown to decrease complications in several surgical fields, offering promise for improving outcomes in undernourished surgical patients [35, 36]. The role for preoperative oral supplementation is still under investigation for urologic surgery.

Related to malnourishment is the clinical entity of sarcopenia. The criteria of sarcopenia is analogous to that of osteoporosis: muscle mass that is two standard deviations below the mean for healthy young reference populations [37]. It is estimated that approximately 20–30 % of the population between 70 and 80 years old

have sarcopenia [38]. From the second to eighth decade of life, almost half of all muscle mass is lost [39]. Muscle loss results from physical inactivity that frequently occurs with aging as well as inflammatory-induced atrophy from increasing co-morbidities [37]. The presence of sarcopenia portends a poor prognosis overall and is associated with significant postoperative morbidity and mortality [40, 41].

Although not a linear relationship between muscle mass and function, they are closely associated. Indices of muscular function, such as gait speed and grip strength, are better at predicting survival and adverse outcomes [42–44]. Loss of muscle mass in the elderly not only negatively impacts functional levels but also cardiopulmonary function, glucose management, and levels of amino acids needed for recovery from surgery [37].

The ratio of muscle to fat is roughly 2:1 for healthy young men, but, this ratio is reversed in the elderly [37]. So, as muscle mass decreases with age, fat mass increases. This can result in a similar BMI despite vastly different body compositions as one ages. If extreme, sarcopenic obesity can occur [45]. The coexistence of sacropenia and obesity in the same individual may result in worse morbidity and mortality than if either condition was present alone [46].

Obesity in elderly patients, even in the absence of sarcopenia, is associated with significant disability and negatively impacts quality of life [47]. Obesity places all surgical patients, regardless of age, at risk for complications [48]. Although weight loss prior to planned surgery may benefit these patients, careful attention is needed for calorie restriction in the elderly to avoid inadequate intake of essential nutrients resulting in malnourishment.

Functional Status

An overall assessment of the geriatric patient's functional status is paramount. Functional state tends to decrease with age, leaving elderly patients with less physiologic reserve to recover from the stress of surgery and to compensate for complications [5, 7]. Functional status includes all physical and cognitive behaviors, which are necessary to maintain independent activities of daily living (ADL) [5]. A patient's overall functional status is often determined by assessing their ability to perform both ADLs and instrumental ADLs [5]. Inability to complete ADLs is associated with an increased risk of postoperative morbidity and mortality [5, 49]. Seymour and Pringle demonstrated that the inability to leave home by one's own efforts at least twice a week was independently associated with a higher risk of major postoperative surgical complications [50]. Functional status is also associated with an increased need for intensive rehabilitation services following surgery [51], including need for nursing facilities upon discharge. Lack of independence on ADLs is also a significant risk factor for readmissions following surgery [49]. Objective measures of functional status, such as gait speed, have also been shown to predict length of hospital stay and discharge status for elderly patients admitted to a geriatric hospital unit [52].

Global Assessment

Recently, the comprehensive geriatric assessment (CGA) has been shown to be a useful predictor of perioperative complications in elderly patients [53]. The CGA allows for a more global gauge of physiologic health as opposed to relying on the chronologic age of a patient. The CGA considers functional status, co-morbid conditions, cognitive functions, psychological state, social support, nutritional status, and geriatric syndromes in the overall assessment of an elderly patient's status [54]. It can therefore act as a robust indicator of the overall ability of an elderly individual to tolerate a major operative procedure. The CGA prior to surgical intervention may improve functional status postoperatively as well as reduce hospital and nursing home stays, potentially decreasing overall costs [55].

Preoperative Risk Assessment

Studies in both the oncologic and non-oncologic settings have demonstrated the CGA to be a valuable preoperative risk assessment tool for elderly patients [5, 55]. However, the American Society of Anesthesiologists Classification (ASA) is the most commonly used system for surgical risk stratification and every patient taken to the operating room is assigned an ASA score [56]. ASA physical status score is an excellent predictor of mortality for elderly patients undergoing prostatectomy [56]. Although ASA is the most widely used preoperative risk assessment tool, it does not have generalizable predictive ability. ASA has been combined with emergency status and procedural risk to develop a Surgical Mortality Probability Model to estimate the 30 day all-cause mortality after surgery [57]. Other co-morbidity scores exist when contemplating surgical risk, including the Charlson Comorbidity Index (CCI) and the Cumulative Illness Rating Scale for Geriatrics (CIRS-G) [55]. CCI has been widely used in urologic literature for both oncologic and non-oncologic surgery [14, 58, 59]. However CCI is limited because it does not factor in the severity of a given co-morbidity. CIRS-G rates the burden of physical illness and should take less than 10 min to complete [60, 61]. Preoperative assessment in elderly cancer patients (PACE) is a comprehensive surgical assessment tool that combines CGA, fatigue level, performance status, and the anesthesiologist's evaluation of operative risk [62]. The team that developed PACE believes it should be used routinely in assessing elderly cancer patients for surgery [62]. Also, whenever assessing geriatric patients for surgery it is important to evaluate for frailty [63, 64]. There are a variety of instruments to measure and objectify frailty, however, to date, there has not been a comparative study to assess which instrument may be superior. Regardless, whatever instrument is used, it is optimal if it assesses both the functional and physical activity of a given patient. If frailty is identified, it may be an indication that medical optimization may be needed prior to surgery [65]. Further research is still required to

determine the best way to incorporate the measurement of frailty into preoperative risk assessment and how to best use the identification of patients with any degree of frailty.

Preoperative Testing

The purpose of preoperative testing is to assess the severity of a known medical condition and to detect unsuspected abnormalities [66]. While routine labs are commonly performed, there is little evidence to support this practice [66]. Most abnormalities would be predicted by history and physical exam and it is rare for abnormal findings to change perioperative care [67, 68]. Considering preoperative testing accounts for an estimated 3–30 billion dollars in annual healthcare costs for the United States [69, 70], some advocate not ordering tests based on age alone, but based on the individual patient and the planned surgery [71].

For cardiac risk stratification, exercise tolerance is a strong independent predictor for postoperative cardiovascular complications [72]. The inability to elevate heart rate above 99 beats per minute during 2 min of exercise, while on a supine bike is predictive of both cardiac and pulmonary complications [73, 74]. Most patients who can exercise greater than four metabolic equivalent of task (e.g., walking at a very brisk pace or carrying clubs while golfing) are at very low risk for cardiopulmonary complications and may not need preoperative cardiac evaluation [75]. Several cardiac risk indices exist for stratification of noncardiac surgery, the most widely used is the Revised Cardiac Risk Index [76–79]. Routine electrocardiogram (ECG) is often obtained for all elderly patients, however ECG is poor at detecting existing CAD as well as predicting postoperative cardiac complications [80, 81]. Regardless, a preoperative ECG can be obtained to provide a baseline for comparison in case of any postoperative event.

Patients with poor overall health status, extensive smoking history, COPD, asthma, and obstructive sleep apnea are at greatest risk for pulmonary complications [75, 82]. A baseline arterial blood gas may be helpful for managing these patients. Smoking is a strong risk factor that is modifiable. Smoking cessation has a physiologic benefit after only 48 h, however, it may take at least 6–8 weeks for a decrease in pulmonary complications to occur [83]. Although all patients should be counseled by their physicians to quit smoking, this is especially true for patients with a history of bladder cancer. Along with all the known health benefits of smoking cessation, continued smoking is associated with an increased risk of recurrence and disease progression in bladder cancer [84–86]. Patients are often unaware of the association between smoking and bladder cancer [87]. Unfortunately, urologists have done a poor job at appropriately counseling these patients on smoking cessation [88] and, often, simple, brief smoking cessation interventions can have important effects on a patient's effort to stop smoking.

Anesthetic Considerations in the Elderly

As with surgical planning, the anesthetic plan for geriatric patients is often more complicated than for younger patients. This complexity results from the increased number of co-morbidities, various medications, poor nutrition, worse functional status as well as the detrimental impact aging has on physiologic function. The cardiac, pulmonary, and renal systems all undergo changes with aging that need to be taken into account when considering a particular anesthetic approach in the elderly.

Cardiac changes frequently found in the elderly patient include a lower sensitivity to beta-adrenergic modulation, altered calcium regulation, and an overall reduction in ejection fraction [89, 90]. Limited cardiac reserve results in a higher risk of hypotension at the time of general anesthetic induction [91]. Maximal heart rate also declines with age resulting in a diminished ability to increase heart rate in response to hypovolemia, hypotension, or hypoxia [4, 91, 92]. Additionally, many elderly surgical patients will have occult CAD, prompting a low threshold for preoperative cardiac evaluation for elective procedures [4]. Diastolic dysfunction is also common in the elderly, and, if severe, it may require arterial pressure monitoring or intra-operative transesophageal echocardiogram monitoring [93].

Pulmonary changes that accompany aging include decreased elasticity of lung tissue and weakened respiratory musculature [91]. Decreased pulmonary elasticity places patients at higher risk of small airway collapse with anesthesia which ultimately results in less efficient gas exchange from decreased alveolar surface area [91].

Renal function and glomerular filtration rate (GFR) also decline with age [94]. Serum creatinine is not a good measure for GFR in the elderly as it often overestimates renal function in this patient population since elderly patients have less muscle mass to produce creatinine. When dosing medications, the overestimation of GFR must be taken into account. Many renally excreted medications, such as pancurium, may need to be avoided in elderly patients. Also, very careful attention must be given to fluid balance since excessive intravenous fluids can easily result in prolonged mechanical ventilation in the geriatric population [95]. Further complicating fluid balance management is the decreased renal concentrating ability and thirst perception that often occurs with aging. This can result in dehydration with consequent electrolyte abnormalities [11].

Changes in body composition also alter the distribution, metabolism, and elimination of drugs [4]. With aging, lean body mass, and total body water decrease while body fat increases [96]. As a consequence, an elderly patient's volume of distribution from water-soluble drugs decreases leading to increased concentrations of these drugs. Fat soluble drugs will have a prolonged action. Hepatic metabolism of drugs also decreases with age, which can contribute to prolonged drug effects [97]. Appropriate adjustments in anesthetic medications must be done to account for the changes in pharmacokinetics and pharmacodynamics with aging.

The choice of anesthetic modality (general or regional) should be selected on a case by case basis taking into account both the operative approach and the patient's ability to tolerate various forms of anesthesia. Regional anesthesia is thought to

have a lower incidence of pulmonary complications [4] because general anesthesia results in decreased airway reflexes which can make an already vulnerable population--the elderly--even more prone to aspiration [98]. However, overall, there is no difference in mortality in patients receiving general or regional anesthesia [4]. Finally, the initial concerns of an association between postoperative cognitive dysfunction and general anesthesia have been proven to be unfounded [4].

Intra-operative Considerations

Appropriate positioning and padding is important for the safety of all patients, especially for the elderly [99]. With aging there is often a reduction in the thickness of the epidermis and subcutaneous tissues, which increases the risk of pressure ulcers and the likelihood of nerve compression [100, 101]. Contributing to this is reduced skin elasticity, which increases the likelihood of damage. It is essential that all pressure points are placed on soft padding [100]. This is especially true if any artificial joints are present as there can be altered sensation and circulation in these areas.

Elderly patients are also less mobile and relatively inflexible compared to younger patients. The prevalence of osteoarthritis is almost 50 % in people 80 years or older [102]. Special care must be taken with positioning and transferring patients with osteoporosis to reduce the risk of iatrogenic fractures. Modifications in the usual procedure position may need to be made for elderly patients. Agreement over the best position and padding should be reached between the surgical team, anesthesiologists, and nursing staff prior to beginning the surgery. Caution should be used when putting elderly patients in trendelenburg, especially at steep angles. There is evidence that steep Trendenlenburg may increase intraocular pressure which places patients with glaucoma at risk for vision loss [103]. Also, Trendelenburg position decreases ventilation and ventricular filling, which may increase the risk of cardiopulmonary complications [104].

Surgical Approach

Laparoscopic surgery may have some advantages over an open approach for elderly patients [3]. The typical quicker overall convalescence, lower narcotic requirements, shorter length of hospital stay, and earlier resumption of diet associated with laparoscopy can greatly benefit the geriatric patient [105, 106]. This must be balanced with the potential for longer surgical time with certain laparoscopic procedures [107]. Increased surgical time is associated with cognitive dysfunction in the elderly [108] and is associated with a higher rate of pulmonary complications [109]. Also, some laparoscopic procedures have a higher rate of intra-operative complications compared to an open approach [106, 109]. Although age alone does not put a patient at a higher risk for a laparoscopic complication, elderly patients are less equipped to

handle a complication when they do occur [15]. The use of robotic assistance may lead to a decrease in the rate of complications [110]. Ultimately, selection of the surgical approach should be based on the individual patient and the comfort of the surgeon.

Reducing Risk of Intra-operative Complications

The rate of cardiovascular complications for urologic surgery is at least 2 % [111]. Between 10 and 40 % of all perioperative deaths are secondary to myocardial infarction [112]. Several perioperative pharmacologic interventions have been used to reduce the risk of cardiac complications. Prophaylatic beta-blockade reduces myocardial demand and prevents an exaggerated postoperative sympathetic response [113, 114]. To avoid the risk of hypotension, stroke, and mortality, lower doses of beta-blockers should be used and then titrated over time [115, 116].

Perioperative statins have also been used given their ability to stabilize coronary plaque and decrease inflammation [117]. Retrospective studies have shown a 38–59 % reduction in morality with statins [118], but no statistical significant difference was seen in a recent randomized control study comparing fluvastatin to placebo [112]. Clinicians must also be aware that abrupt discontinuation of statins, such as being NPO before and after surgery, can result in a paradoxical withdrawal state that leads to worse cardiovascular outcomes [119]. Interestingly, a recent systematic review has suggested that statins may also reduce the rate of gastrointestinal and infectious complications after abdominal surgery [120], however, prospective trials are needed before any definitive conclusions/recommendations can be reached.

Continuation of aspirin and other anti-platelet medications in the perioperative period can significantly reduce the risk of cardiovascular complications [121], but the continued use of these medications need to be balanced against their increased risk of bleeding. In general, patients with cardiac stents should be continued on aspirin unless bleeding risk is too great [122]. Patients on aspirin for primary prevention of acute coronary syndrome, who are at a low risk of perioperative cardiac complications, can usually have their aspirin held a week prior to surgery [122].

It is generally recommended that perioperative glucose levels be maintained around 110 mg/dl to avoid perioperative complications [123]. Although this glucose target may need to be shifted upwards for certain individuals at greater risk of hypoglycemia from treatment with insulin [124]. Reducing preoperative fasting time can also reduce the risk of hypoglycemia [125]. Preoperative carbohydrate-based drinks that are taken up to 2 h before surgery improves insulin sensitivity, preserves structural proteins, and improves patient comfort [126].

Perioperative hypothermia is a common occurrence in the operating room that must be avoided in geriatric patients [127]. Hypothermia depresses cardiac function and prolongs recovery from anesthesia [128]. Perioperative hypothermia is also associated with poor wound healing, increased incidence of surgical-site infections,

and patient discomfort [129]. Hypothermia often results from a cool ambient temperature and use of cold intravenous fluids, especially blood product transfusions [128]. These effects can be minimized by forced-air warming and the use of a fluid warmer [127].

Postoperative Management

There has been recent interest in the development of objective measures to assist surgeons in postoperative decision-making [130]. Since the elderly handle anesthetics differently than younger patients, the surgeon should discuss with the anesthesia team the plans for discharging or admitting an elderly patient from the post-anesthesia care unit, even if it was a short uneventful procedure [131, 132]. While discharge criteria following ambulatory surgery has existed for several decades [133], only recently has attention been given to finding an accurate objective post-operative assessment tool for major surgeries [130]. Clearly, determining risk for postoperative complications is useful for deciding on level of care needs [134]. Similar to the selection of surgical candidates, age alone should not be the sole determinant for admission to the intensive care unit [135, 136]. The Physiological and Operative Severity Score for the enUmeration of Mortality and morbidity (POSSUM) and the Acute Physiology and Chronic Health Evaluation (APACHE II) scores are commonly used predictors of postoperative risk. However, both the POSSUM and APACHE II scores are complicated calculations that can be challenging to perform in a busy clinical setting. The Surgical APGAR score is a simpler predictor of complication, using three intra-operative measures; maximal heart rate, lowest mean arterial pressure, and estimated blood loss [134]. A modified version of the Surgical APGAR has been described for radical cystectomy patients [137]. Efforts to improve the predictive ability of these risk scores will likely focus on customizing them to specific procedures and patient populations [138]. These objective measures will likely become of increasing importance in high risk patients, such as the elderly.

Interest in postoperative clinical care pathways for many major urologic procedures has also increased recently [139, 140]. Clinical pathways provide a framework to optimize care to improve outcomes while being more cost-effective. While these clinical pathways can certainly be applied to the geriatric population, some modifications may be needed [141]. For example, patients should be restarted on their home medications as soon as it is safe from a surgical standpoint, particularly those patients on medications for neurologic and/or cardiac conditions. For example, even a few hours without levodopa can cause a return of Parkinson's disease symptoms [142].

Pulmonary complications are common cause of morbidity for the elderly. Postoperative functional residual capacity can decrease by up to 70% and remain depressed for 1 week after surgery [4]. This could be improved with lung expansion by

encouraging incentive spirometry, coughing, and deep breathing exercises. Preoperative education on spirometry and coughing may improve the effectiveness of these interventions [143]. Another strategy to decrease the risk of pulmonary complication is early ambulation, which improves ventilation and secretion clearance [144]. Early ambulation may also hasten the return of bowel function and prevent postoperative ileus [145]. It is critical to limit bed rest for elderly patients to avoid skeletal muscle de-conditioning, which could result in a loss of independence and the need for discharge services [146].

Early ambulation also decreases the risk of deep venous thrombosis (DVT) and pulmonary embolism (PE) from developing [147]. Along with sequential compression devices, another cornerstone of DVT/PE prevention is pharmacologic prophylaxis with subcutaneous heparin or low molecular weight heparin for select patients [147]. Unfortunately, adherence rates with pharmacologic prophylaxis in perioperative patients are suboptimal [148]. Urologists should be aware of and adhere to the American Urologic Association's best practice statement for venous thromboembolism prevention [149].

Traditionally, postoperative oral feedings were not begun until the return of bowel function as demonstrated by flatus due to surgeons' fear of postoperative ileus or anastomatic disruption [150]. This dogma has been challenged, and numerous studies have shown a benefit to early oral feedings, even in the setting of recent intestinal anastomosis [34, 150]. Geriatric patients would particularly benefit from early intake of nutrients to assist in postsurgical recovery. Early resumption of oral intake also reduces the risk of electrolyte and fluid imbalances to which elderly patients are more prone [151]. Maintenance of homeostasis is complicated by the physiologic changes of aging such as GFR reduction and changes in neurohormonal regulation of electrolytes and water, which can be disrupted during the perioperative period [151]. Fluid management for the elderly should begin before surgery with consideration of a shortened preoperative fast. Evidence supports a reduction of fasting time improves outcomes without increasing anesthesia risk [33, 152].

Postoperative pain is an important issue for elderly patients. With aging, there is a reduction in the efficacy of endogenous analgesic systems [153]. However, pain is often undertreated in the elderly, likely from the clinician's underestimation of pain and their fear of adverse events. Given the decreased drug metabolism and clearance in the elderly, narcotics and sedatives should be given with caution. Nevertheless, under-treatment of pain not only leads to unnecessary patient suffering, but can also increase the risk of postoperative delirium [154]. The use of patient-controlled analgesia has been used successfully in the postsurgical geriatric population to provide adequate pain control that is titrated to a safe level [155, 156]. To further reduce the need for opioids, a multimodal analgesia approach with epidurals, acetaminophen, and NSAIDs can be considered [157]. Alternatively, a patient-controlled analgesia epidural with local anesthesia not only achieves effective pain control, but it also reduces systemic opioid consumption and improves mental status and bowel activity [156].

Special Considerations for the Elderly After Surgery

Delirium is a common, underappreciated complication in the postoperative geriatric population. Delirium is associated with increased morbidity, functional decline, and greater length of hospital stay [158]. It increases the overall cost of hospitalization as well as resource utilization by increasing the need for inpatient nursing care and nursing home placement at the time of discharge. Most importantly, delirium is associated with high rates of mortality [158, 159]. The rate of delirium after major urologic abdominal surgery is estimated to be between 11 and 21 % [3], however delirium is often under-recognized by nurses and physicians [160, 161].

Prevention is the key to delirium treatment and begins with the elimination of unnecessary drugs, especially sedatives, narcotics, and anti-cholinergic medications [158]. Risk factors for postoperative delirium include age, dehydration, electrolyte abnormalities, immobilization, and preoperative dementia [75]. As such, pain control, oxygen levels, electrolytes, and fluid balance should be optimized [75]. Patients should be provided their glasses and hearing aids as needed. The patient's room should be well lit with an appropriate level of sensory stimulation during daylight hours. For a patient at high risk of delirium, a consultation with a geriatrician should be considered. A randomized controlled study of elderly patients with hip fractures showed that a proactive geriatrics consultation reduced the rate of delirium from 50 to 32 % [162]. The severity of these episodes was also decreased. If delirium does develop, the use of restraints should be avoided. Also, it is important to consider that delirium may be a symptom of another underlying pathophysiologic process, such as an infection or myocardial infarction, which should be ruled out [75].

In general, geriatric patients are at greater risk of aspiration due to decreased oropharnygeal protective reflexes associated with aging [98]. Dysphagia, dementia, poor oral hygiene, and multiple comorbidities are risk factors for aspiration pneumonia [163]. Aspiration precautions should be taken for high risk patients, especially for those with neurologic conditions such as dementia or Parkinson's disease [129].

Finally, patient falls are another concern common to the geriatric population and they are associated with an increased risk of subsequent death [164, 165]. Falls result from susceptible individuals being in a hazardous environment. Age associated changes in posture and decreased muscle strength increase vulnerability [166]. Impairment of gait, balance, vision, cognition, and function are also risk factors [166]. Another risk factor for elderly falls is lower urinary tract symptoms, especially nocturia and urge incontinence [167]. Use of anti-cholinergic medications also increases fall risk [168]. Patients with a history of falls are more likely to fall again [166]. A post fall anxiety syndrome may develop which results in self-imposed restriction in ambulation and activity [169]. Screening for fall risk and nursing assistance whenever getting out of bed are the cornerstones of prevention.

Discharge Planning

Discharge planning should begin prior to admission for all patients, but especially for geriatric patients. Early discharge planning also assists in obtaining needed resources, such as acute rehabilitation facilities, which are commonly needed for elderly patients. Making these arrangements as soon as possible allows for an efficient hospital discharge and avoids delays in finding placement. A discussion about advance directives and healthcare proxy should especially occur with all elderly patients. Information on co-morbidities, functional status, and nutritional state obtained during the preoperative assessment will be important to help determine post-operative placement needs. Consideration of social support, such as marital status, living situation, and potential caregivers, must also be factored into disposition planning. A recent Cochrane review showed that individualized discharge planning reduced length of stay and risk of readmission for elderly patients [170]. Discharge planning should focus on patient participation and education [171]. Outpatient education prior to surgery is particularly beneficial to elderly patients, who may have difficulty remembering information when in pain and on pain medications [172].

Patients with urinary diversions should have early follow-up with a stoma care specialist to optimize care and improve quality of life [173]. Family members and care givers should be encouraged to attend because many patients do not care for their urostomy independently [174]. For these type of patients, there has been a shift towards decreasing the patient's length of hospital stay in favor of increasing utilization of subacute care facilities and home health services [175]. Geriatric patients are at an increased risk of need for healthcare services at discharge. For example, older age as well as, lower preoperative albumin, unmarried status, and the presence of co-morbidities were predictors of the need for home health services after radical cystectomy [176]. While older age, poor preoperative exercise tolerance, and longer hospital stay were potential risk factors for facility placement after radical cystectomy [176].

Prior to the patient's discharge, adequate communication with their outpatient geriatrician or primary care provider is important to ensure an appropriate transition of care. During the first few weeks following transurethral resection of the prostate, it is common for patients to contact their primary care provider with treatment-related concerns [177]. Similarly, despite claiming to be very satisfied with teaching and information provided at discharge, many men will still use community healthcare resources following prostatectomy [178]. For geriatric patients on multiple medications, transition from an inpatient to outpatient setting must be well coordinated with their outpatient provider to reduce the risk of medication and laboratory monitoring errors [179]. At discharge, geriatric patients should be encouraged to follow-up with their primary care provider to help reduce the risk of readmission [180].

Conclusion

The elderly population in the United States continues to grow in size. Advances in surgery and anesthesia have allowed for elderly patients to undergo operations that may not have been possible a couple of decades ago. Clearly, chronologic age should not be a contraindication for any surgery, and a patient's physiologic age needs to be considered. The optimal perioperative care of elderly surgical patients begins with a comprehensive preoperative assessment. Perioperative management and discharge planning should be individualized to achieve the best possible outcomes for the patient.

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Chapter 6
Complications Particular to the Elderly

Benjamin L. Taylor and Thomas J. Guzzo

Introduction

With advances in medical care and increasing life expectancy, the treatment options for elderly patients are both vast and evolving, combining both medical and surgical alternatives. The potential to both cure and improve the quality of life in this patient population is immense. People over the age of 85 are the fastest growing age class in our society today [1]. Those patients 65 years old and older are expected to be 20 % of our population by 2025 [2]. More than half of these individuals will undergo major surgery, most after the age of 50 [2]. These patients are more likely to have cardiopulmonary disease, diabetes, and other health problems and are more likely to have elective surgery canceled [1, 2]. This patient population is more likely to present with advanced disease, require emergent surgery, and also has higher mortality when compared to younger patients [1, 2].

Operating on the elderly isn't without increased risk. The 30-day mortality increases by nearly 10 % for every year over age 70 [3]. Those patients with an increased *ASA* (American Society of Anesthesiologists') score and decreased albumin are at increased risk of postoperative complications and mortality [3]. The National Surgical Quality Improvement Program showed the 30-day mortality for patients over the age of 80 was 8 % and the surgical complication rate was 20 % [3]. A recent retrospective study looking at Medicare claims showed that dementia, hospitalization within 6 months before surgery, and post-operative complications were independently associated with worse 1-year survival [4]. Another study of patients over 70 years of age undergoing surgery found a 20 % complication rate within 5 days and a 6 % mortality rate within the first 30 days. This same study also found many patients had more than one complication for

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an average of 31 complications per 100 patients [3]. The incidence of these complications affects morbidity and mortality. The primary goal should be to prevent complications rather than treat them. However, when a complication does occur, it must be recognized and dealt with expeditiously and vigilantly to prevent further harm to the patient, particularly in the elderly population who often have less functional reserve. Some of the most common and severe complications to affect the elderly population are deep vein thromboembolism, functional loss, immobility, delirium, postoperative cognitive dysfunction, urinary tract infection, falls, and frailty.

Deep Vein Thrombosis

When compared to younger patients, elderly patients are at increased risk of pulmonary venous thromboembolism with greater associated morbidity and mortality [5]. To understand why this population is at increased risk, it is important to remember the main factors contributing to venous thromboembolism as indicated in Virchow's triad: venous stasis, hypercoagulability, and intimal injury [5]. According to the literature, immobility is the most prevalent risk factor for pulmonary embolism [5]. Elderly patients, especially those with frailty (see below), are more likely to be immobile in the postoperative period, and this venous stasis puts them at a higher risk for these events. A prospective cohort study demonstrated a significantly increased risk for VTE in patients greater than 80 years old compared to less than 80, and among those greater than 80 years old, there was a higher 30-day mortality associated with VTE complication [6]. Elderly patients are more likely to have heart failure [7] and heart failure is a risk factor for thromboembolism as demonstrated by the MEDENOX trial, which showed that 15 % of patients with class III or IV heart failure treated with placebo had episode of VTE [8]. Also, anesthesia leads to venous dilation and, therefore, venous stasis, thus also making it a risk factor for thromboembolism [5].

Elderly patients also have less fibrinolytic activity in leg veins than in arm veins, further increasing the likelihood of forming deep venous thromboembolism [5]. This population has higher fibrinogen levels and higher procoagulant factors when compared to a younger population [5]. All of these factors put the elderly patient at increased risk for venous thromboembolism.

The most significant complication of DVT is pulmonary embolism (PE), which occurs more frequently in the elderly population [5]. Those patients experiencing dyspnea, tachycardia, tachypnea, and chest pain must be evaluated immediately to rule out an underlying PE. The incidence of PE is 1.8 % in those aged 65–69, but increases to 3.1 % in the 85–89-year-old population. When compared to age 20, an 80-year-old is 200 times more likely to have a PE [5]. Not only is PE more prevalent among the elderly population, this diagnosis also carries more morbidity and mortality as well. When compared with the general population, the elderly are six times more likely to die of a pulmonary embolism [5].

Duplex ultrasound is the most commonly used study to evaluate for DVT; however, this study is most accurate when the patient has symptoms of lower extremity DVT. In the absence of symptoms, duplex ultrasonagraphy remains a very specific

test. MRI with gadolinium is both sensitive and specific for DVT, but can be more difficult and expensive to obtain than a venous Doppler [5]. Contrast venography is not used as often, but does remain the gold standard. The best treatment for DVT is prevention. DVT prophylaxis with low dose heparin or low molecular weight heparin are viable options [5].

Functional Loss/Immobility

The elderly patient faces significant barriers to postoperative mobility including increased incidence of arthritis, musculoskeletal problems, and quicker debilitation when compared to younger patients [2]. Prolonged bed rest in this population leads to significant pathophysiological complications in multiple organ systems [2]. The skin can be extremely affected by immobility in the form of pressure ulcers, which are associated with increased mortality [2]. Osteoporosis, by way of bone resorption, occurs at a faster rate in immobilized patients and increases fracture risk [2].

Sarcopenia, loss of muscle mass, is of vital concern in this population, especially when it is combined with frailty and disability. It leads to poor muscle quality, decreased balance, gait speed and muscle strength [9]. In hospitalized patients, sarcopenia increases the risk of complications such as pressure ulcers, infections, institutionalization, loss of autonomy, poor quality of life, and mortality [10]. Therefore, this population should be involved in early mobilization programs and postoperative physical therapy programs [11]. A nutrition team should also be involved to help optimize the patients' diet to prevent muscle loss, and if patients are unable to tolerate oral feeding, tube feeds or parenteral feeds should be initiated [11].

Immobility also leads to increased risk for deep venous thromboembolism, pneumonia, aspiration, and atelectasis [2]. Immobility can lead to alterations in cardiac function such as hypotension and stroke [2]. The gastrointestinal system is also significantly affected by immobility, leading to decreased appetite and dehydration which can further exacerbate constipation and fecal impaction [2]. Immobility also affects cognition by leading to depression, altered sensorium, and loneliness [2]. Many of these complications are prevented by early mobilization and the work of a multidisciplinary team including nurses, physical therapists, family members, occupational therapists, physicians, and the patient's participation [2].

Mental Disorders Associated with Aging

Delirium

Postoperative delirium, defined as incoherent speech, altered orientation, attention, emotional lability, and memory lapse for a short time period, accounts for longer hospital stays, increased cost, increased morbidity, mortality, and delayed functional recovery [1, 2, 12, 13]. This post operative complication costs over $4 billion

per year [13]. Twenty percent of elderly surgical patients may experience postoperative delirium [2]. Delirium, which is usually reversible, tends to affect this patient population more in the evening hours and after postoperative day 1, peaking between postoperative days 2–7 [1, 13].

There are a multitude of general risk factors for postoperative delirium, including age, preoperative cognitive function, ASA > II, medication interactions, withdrawal from medications being held in the postoperative period, alcohol withdrawal, insomnia, depression, dementia, anxiety, deficiencies in vision or hearing, and physical impairment [1, 2, 13]. Operation specific risk factors also contribute to postoperative delirium. The degree of operative stress is directly proportional to the risk of postoperative delirium, such that high stress procedures such as vascular surgery have a delirium risk of 36 % but low stress procedures, such as cataract surgery, have a delirium risk of 4 % [12].

Intraoperative events which may lead to delirium include reduced oxygen delivery to the cerebral tissue such as: major blood loss, decreased hemoglobin, arterial hypoxemia, and hypotension [1, 2, 13]. One proposed mechanism for this condition is that reduced oxygen delivery to the brain alters the neurotransmitter milieu in a detrimental fashion [13]. Surgery is known to cause alterations in stress hormone homeostasis which may also alter this milieu, possibly leading to delirium [13]. Delirium may also increase the risk of more significant complications such as heart attack and pneumonia [2]. Interestingly, the type of anesthesia does not appear to have an effect on the incidence of postoperative delirium [1, 13, 14].

Metabolic abnormalities during surgery can also play role in postoperative delirium [13]. Specifically, alterations in sodium, carbon dioxide levels, and overall fluid status, namely dehydration, are known to contribute to postoperative delirium. Pharmacokinetics vary widely among the elderly population which makes predicting response and clearance of anesthestic challenging. Perioperative anesthetic still present in the postoperative period likely contributes to postoperative delirium as well [13].

The clinician's focus should be on prevention rather than the treatment of postoperative delirium. Medical illnesses should be optimized prior to surgery and an up to date medication reconciliation should be done [13]. The patient should have adequate cerebral oxygen supply preoperatively and be adequately hydrated. An accurate drug and alcohol history should be obtained in order to identify and prevent postoperative withdrawal. Those patients with a history of alcohol abuse should be placed on thiamine to prevent Korsakoff's psychosis [13]. A proper postoperative pain control plan should be identified and carried out. The patient should be provided cerebral stimulation, optimal resting and sleeping conditions such as reduced noise levels, frequent orientation by the staff/family, easy access to visual aids like glasses, hearing aids, and early mobilization [12, 13]. These protocols may decrease postoperative delirium by 5 % [12]. Clocks, calendars, windows, and appropriate daytime/nighttime lighting may also help keep the patient oriented [2]. The patient's electrolytes, oxygen levels, blood pressure, and fluid status should all be maintained appropriately in the perioperative and postoperative period [12, 13]. Tubes and drains should be managed vigilantly and removed as soon as possible as they have also been linked to postoperative delirium [12].

Once postoperative delirium occurs, it must be recognized in order to be treated appropriately. Up to half of delirium cases may be missed by the primary team [12]. Delirium must also be distinguished from postoperative cognitive dysfunction (POCD), which only affects memory, attention, and comprehension [12]. There are three main types of delirium: hyperactive, hypoactive, and mixed. Hypoactive delirium is the most common (71 %), followed by mixed delirium (29 %), while hyperactive is rare [12]. The hypoactive type of patient may be lethargic, unaware of his/her surroundings, and have decreased alertness [12]. The patient with hyperactive delirium has symptoms of irritability, agitation, restlessness, and may even be combative. The patient with mixed delirium has a combination of hypoactive and hyperactive delirium [12].

The Confusion Assessment Method (CAM-ICU) is a common test used to diagnose delirium in hospitalized patients (see Fig. 6.1) [12, 13]. This method provides a standardized system with high validity and reproducibility [12, 13]. CAM-ICU not only examines mental status, thinking, and attention, but also level of consciousness. This assessment method can be used by both nurses and clinicians [12].

Treating postoperative delirium should focus on identifying risk factors, as well as underlying conditions, and treating them appropriately. A thorough history and physical should be done first [12]. Postoperative complications, including urinary

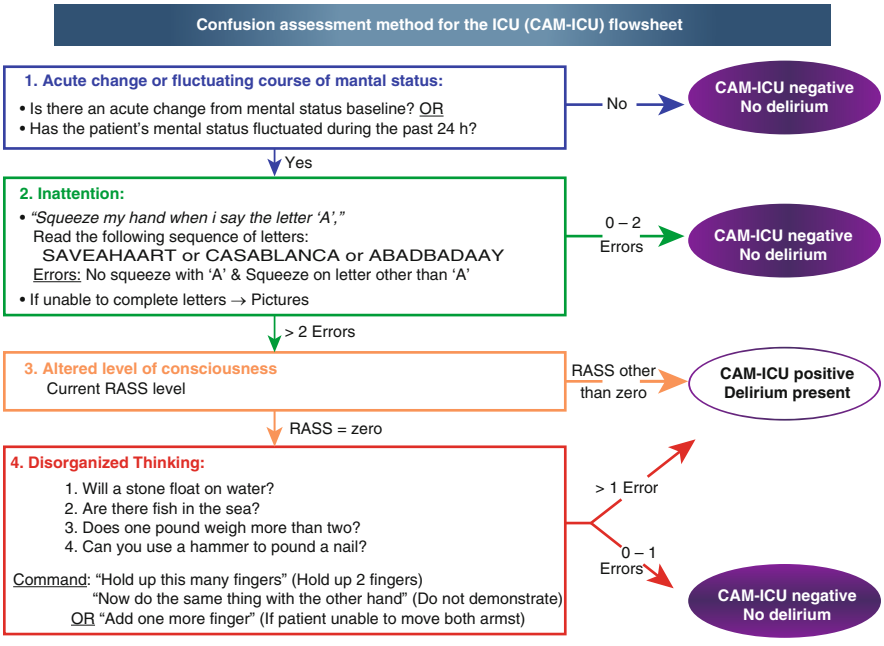
Confusion assessment method for the ICU (CAM-ICU) flowsheet
1. Acute change or fluctuating course of mantal status:
• Is there an acute change from mental status baseline? OR
• Has the patient's mental status fluctuated during the past 24 h?
No
CAM-ICU negative
No delirium
Yes
2. Inattention:
• "Squeeze my hand when i say the letter 'A'," Read the following sequence of letters:
SAVEAHAART or CASABLANCA or ABADBADAAY
Errors: No squeeze with 'A' & Squeeze on letter other than 'A'
• If unable to complete letters → Pictures
0 – 2 Errors
CAM-ICU negative
No delirium
> 2 Errors
3. Altered level of consciousness
Current RASS level
RASS other than zero
CAM-ICU positive
Delirium present
RASS = zero
4. Disorganized Thinking:
1. Will a stone float on water?
2. Are there fish in the sea?
3. Does one pound weigh more than two?
4. Can you use a hammer to pound a nail?
Command: "Hold up this many fingers" (Hold up 2 fingers)
"Now do the same thing with the other hand" (Do not demonstrate)
OR "Add one more finger" (If patient unable to move both armst)
> 1 Error
0 – 1 Errors
CAM-ICU negative
No delirium

Fig. 6.1 Confusion assessment method (Courtesy of Vanderbilt University. Available from: http://www.mc.vanderbilt.edu/icudelirium/docs/CAM_ICU_flowsheet.pdf) (Copyright @ 2002, E. Wesley Ely, MD, MPH and Vanderbilt University, all rights reserved)

tract infection, pneumonia, electrolyte disorders, hypotension, hypoxemia, and fluid imbalances can also lead to postoperative delirium and should reflexively be ruled out upon recognition of the patients altered mental status [1, 2]. This can be achieved through checking electrolyte levels, magnesium, phosphate, calcium, arterial blood gas, hemoglobin level, blood cultures, urine culture, urinalysis, and a chest X-ray [12, 13]. The clinician must remember infection presents differently in the elderly population and may not present with leukocytosis and fever, but may present primarily with delirium [12]. Fluid status as well as overall nutritional status should be checked and corrected [13]. The above parameters (electrolytes, oxygenation, etc.,) should be optimized upon recognition of postoperative delirium to begin supportive care and encourage expeditious recovery [13].

Medications and polypharmacy also contribute to postoperative delirium [12]. Anticholinergic medications and benzodiazepines should be avoided when possible [2]. Anticholinergic pharmaceuticals, as well as those drugs with anticholinergic side effects, are well known to contribute to postoperative delirium. However, those patients taking benzodiazepines prior to surgery must be kept on them in the postoperative period to prevent benzodiazepine withdrawal, which can also cause delirium [13]. Other medications known to contribute to delirium include: "cimetidine, corticosteroids, diphenhydramine, belladonna, promethazine, warfarin, narcotics, and antiparkinsonian drugs" as well as morphine [12]. These medications should be minimized when possible. Poor postoperative pain control can also contribute to postoperative delirium and should be prevented [13].

Once postoperative delirium has been diagnosed, patient safety becomes paramount. Those patients with hyperactive or mixed delirium will be prone to pull at lines and tubes [12]. Hypoactive delirium may present with wandering patients unaware of what he/she is doing [12]. Delirious patients are also at risk for falling and may be unable to protect themselves from themselves [12]. These patients should be monitored more closely with one-to-one surveillance or transfer to a higher acuity setting such as a step down unit or ICU [12]. If initial maneuvers to calm the patient fail and the patient continues to be a danger to themselves, restraints and pharmacologic therapy should be instituted [12]. Haldol, the pharmacologic therapy of choice for delirium, may help keep the patient protected from falling or hurting themselves as a result of delirium [2, 12, 13]. Haldol dosing is dependent upon patient placement in the hospital [12]. Those patients in the ICU should receive a loading dose of 2 mg intravenous with another 2 mg given every 15–20 min until the delirium abates [12]. Once controlled, delirium can be maintained prophylactically with scheduled doses. Once on the ward, Haldol should be initially dosed at 1–2 mg with 0.25–0.5 mg every 4 h [12]. The side effects of this medication are extrapyramidal side effects and prolonged QT syndrome. Periodic EKG's should be monitored while the patient is on this medication [12]. Also, any preoperative metabolic abnormalities, especially those involving sodium, should be corrected prior to surgery if possible [2, 13].

Postoperative Cognitive Dysfunction

Postoperative Cognitive Dysfunction, or postoperative memory or thought impairment, difficulty with social integration and or executive function slowing of information processing speed, language impairment, and changes in personality, have been described more frequently among the elderly population [13, 15, 16]. This symptom complex manifests as difficulty multitasking, short-term memory problems, attention or focusing problems, and trouble "finding words" [16]. POCD does not involve alterations in sensorium or consciousness like delirium and also tends to be longer lasting. POCD leads to difficulty in maintaining activities of daily living and tends to affect the patient after he/she is discharged from the hospital, unlike delirium which is mainly an intra-hospital event [16]. POCD results in longer hospital stays, more nursing care, increased cost, and may increase mortality.

The majority of research on POCD has been in the field of cardiac surgery where up to 50–80 % of patients may experience POCD, and up to 20–60 % of these patients may continue to experience POCD months after surgery [13, 16]. The incidence of POCD in those patients undergoing major noncardiac surgery is 23 % among 60–69 year-olds and 29 % in those patients over age 70. Up to 14 % of patients older than 70 continued to have symptoms of POCD 3 months after surgery [16]. Up to 1 % of POCD patients may have POCD symptoms last over 1 year from the date of surgery [16].

Severity of surgery also contributes to POCD. Those elderly patients undergoing minor surgery experienced POCD at a rate of 7 % [16]. Patients who underwent surgery and were discharged home the same day also had a low incidence of POCD [16].

POCD is a multi-factorial disorder with poorly understood risk factors, but potential causes include age, type of surgery, anesthetic drugs used, decreased preoperative cognitive status, infection, preoperative medications, preoperative depression, comorbid conditions, intraoperative hypothermia, intraoperative hypotension, intraoperative hypoxia, intraoperative abnormalities in blood glucose, and duration of surgery [13, 15, 16]. However, age is the most important component of POCD [16].

The diagnosis and existence of POCD is clear, however, the exact causation is still being studied. There are several current theories attempting to explain the occurrence of POCD. One such hypothesis is linked to cognitive reserve, where increased reserve may be protective of POCD. This theory is born out of evidence that patients with higher educational level have less POCD [16]. However, it is unclear whether the protection comes directly from higher education or a difference in those patients' brains that pursue higher levels of education. Other theories include the type of anesthetic gas used, however, these theories have been opposed by several studies showing type of gas may not contribute to POCD [16]. However, further studies have shown anesthetic agents can affect postoperative cognitive function, but the deficits rarely last beyond 2 weeks and some agents may even be neuroprotective [16].

Intraoperative hypoxia and hypotension were once thought to contribute to POCD [16]. However, current studies show POCD isn't prevented by guiding oxygen therapy by pulse-oximetry [15, 16]. Studies also show that perioperative hypotension, determined by mean arterial pressures, likely does not contribute to POCD [15, 16]. Intraoperative hyperventilation and hypocapnia seem to cause prolonged reaction times and may contribute to POCD [15]. Interestingly, it appears the type of anesthesia may have no affect on POCD, but debate among the literature exists [13, 15]. It is difficult to isolate the type of anesthesia as a cause because controlling for all other surgical factors such as blood pressure can be difficult [15].

As previously mentioned, POCD incidence is dependent on degree of surgery which leads investigators to examine surgery as the cause of POCD [16]. Surgery causes an inflammatory response leading to cytokine release and neuroendocrine hormone release. The surgical stress response is less pronounced in patients undergoing minor surgery [16]. There are reports of inflammatory mediators and cortisol levels being related to delayed functional recovery [16].

The assessment and treatment for POCD mirrors that of assessing cognitive status in the nonoperative patient. These tests include the mini-mental status exam, clock-drawing test, and list learning test [16].

As with most other complications, prevention is the best the form of treatment. Preventing hypothermia, perioperative hypotension, oxygen therapy, proper pain control, emotional support, and frequent assessments are the best ways to prevent POCD [16]. Currently, there are no treatment guidelines for POCD and there is no evidence to suggest treating POCD once diagnosed has any effect on the outcome [13].

Urinary Tract Infection

Urinary tract infections (UTI) can be a challenging entity in the way the symptoms manifest in the elderly and the management associated with them. There are differences in management between males and females, those with recurrent infections, and those with indwelling catheters [17]. Patients may present with symptoms comparable to their younger counterparts such as urgency, dysuria, and frequency, or their only presenting symptom may be confusion [2, 18]. Those patients with indwelling catheters may not have these symptoms [18]. Also, many symptoms of UTI can be chronic in this population and discerning symptoms of the aging urinary tract from those of infection may be challenging. These symptoms become more difficult to assess in patients with cognitive deficiency, which can lead to a delay in diagnosis [18]. Altered sensorium, agitation, further cognitive decline, restlessness, confusion, falls, lethargy, and emotional instability may also indicate pain in this population, which should be further evaluated as suprapubic pain, costovertebral angle pain, and/or flank pain may be secondary to UTI. Changes in urine characteristics may also indicate UTI [18]. While cloudy and foul smelling urine is not diagnostic of a UTI, it should prompt further examination [18]. New onset gross

hematuria can also be alarming in the postoperative period. There are numerous causes for this including recent instrumentation, indwelling catheter, bladder cancer, and infection as well as several others [18]. However, new onset hematuria in the postoperative patient that presents well after the Foley catheter was placed or removed merits further examination. New onset urinary incontinence can also be a sign of UTI and should prompt further evaluation with urinalysis and culture [18]. The populations at increased risk of presenting with vague or minimal symptoms are those with indwelling catheters, baseline incontinence, those receiving analgesics or antipyretics, the immunocompromised, and/or cognitively impaired [18].

Less specific symptoms may also be caused by UTI in the elderly population. Fever may be the only indicator of UTI in this population as well, and a urinalysis with culture is a standard part of the postoperative fever evaluation. The patient with UTI may also present with hypotension and/or tachycardia [18]. Tachypnea, rales, respiratory distress, nausea, vomiting, and abdominal pain can also be symptoms of UTI in this population [18]. Indwelling urinary catheters are an obvious risk factor for UTI [2]. Elderly patients may be more likely to have a catheter secondary to hindered mobility, incontinence, and medication-induced retention [2]. Foley catheters should be removed as soon as possible to minimize the risk of UTI.

Falls

Risk factors for falls include age, cognitive impairment, impaired mobility, and functional impairment [19]. A simple clinical assessment can identify elderly patients who are at greatest risk for falling [20]. Cognitive impairment as well as prevention thereof has been thoroughly discussed in this chapter. Impaired mobility and functional impairment can be prevented by exercise, early mobilization, and balance training [19].

Frailty

Understanding the concept of frailty is essential due to the advancing age of the population and its intrinsic relationship with poor health care outcomes. While there are various interpretations of frailty, it may be best conceptualized as an age-related, multi-dimensional state of decreased physiologic reserves that result in diminished resiliency, loss of adaptive capacity, and increased vulnerability to stressors [21]. This increased vulnerability to complications puts patients at risk for hospitalization, falls, disability, and death. Although there is agreement on definitions and concepts of frailty, there is no consensus for which tool is best to use for assessing frailty, or the capacity each measured variable can predict poor outcomes [22].

There are two common tools that are utilized when studying frailty in the literature. The first is the phenotypic definition of frailty, which operationalized a

screening tool incorporating physical measures such as grip strength weakness, slow walking speed, unintentional weight loss, self-reported exhaustion, and low activity levels [23]. The other tool is the accumulation of deficits definition of frailty, which views frailty as an accumulation of medical, functional, cognitive, and social deficits that are acquired, associated with increasing age and adverse health outcomes [21, 24]. In other words, phenotypic, or biologic frailty causes the physical manifestations of frailty while deficit accumulation frailty is caused by accumulated abnormal characteristics or deficits [21].

In the postoperative patient, frailty leads to more complications, increased length of stay, and increased likelihood of being discharged to a rehabilitation facility rather than to home, Fig. 6.2 [11, 25]. In addition to increased risk of postoperative delirium, frailty also puts patients at increased risk for deep venous thrombosis in the postoperative period as a result of increased d-dimer and factor VIII levels that increase with age as well as in the postoperative state by in flammatory mediators, Fig. 6.2 [11]. Intermittent pneumatic compression devices should be used until patients are sufficiently ambulating [11]. For patients who have mild to moderate risk of DVT, low-dose unfractionated heparin 5000 units twice daily or low molecular weight heparin <3400 units daily should be used. For those patients at high risk, low dose unfractionated heparin 5000 units three times per day or low molecular weight heparin >3400 units daily should be used [11].

Frailty can be used as a prognostic factor as well. Those patients who exhibit frailty have higher mortality rates, hospitalization rates, and decreased functional

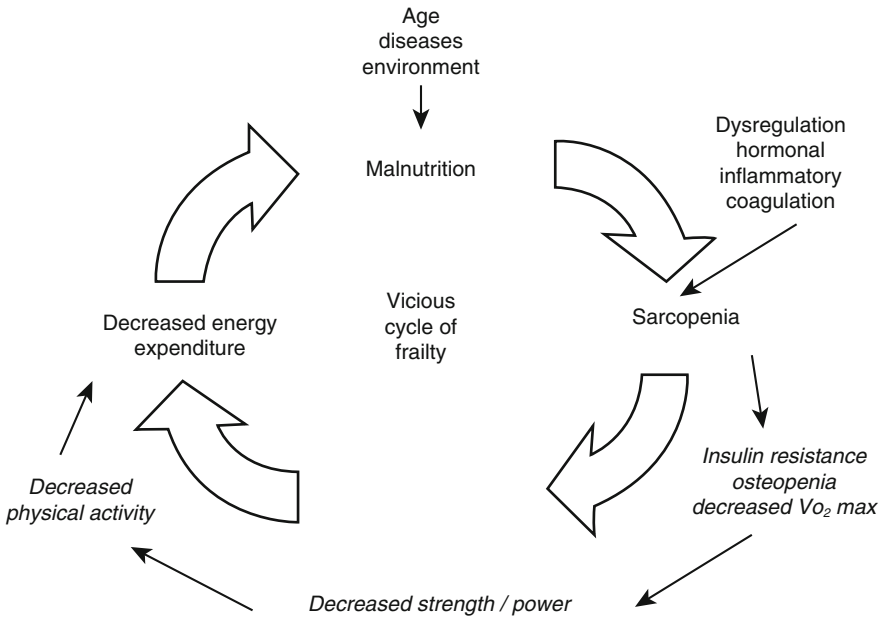

Fig. 6.2 Cycle of frailty (Adapted from McDermid et al. [25])

outcomes [25]. A multifocal approach, including preoperative risk assessment, exercise, nutrition, anesthesia type, team-based pathways, delirium prevention and palliative care approaches are needed to treat and prevent frailty [21]. However, the extent to which frailty scores will play a role in preoperative assessments and enhance clinical outcomes remains unanswered.

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Chapter 7
Urologic Oncology

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Surgical Considerations in Elderly Cancer Patients

Approximately half of all surgical procedures in the U.S. are performed in patients ≥65 years of age [1]. Furthermore, 50 % of new cancer diagnoses are made in patients ≥70 years of age [2]. Many elderly patients have complex physiologic and functional issues which merit consideration when considering surgical intervention.

The aging process is associated with changes in many organ systems that can impact an elderly patient's ability to withstand and tolerate a major surgical procedure. The renal, cardiac, immune, hepatobiliary, and pulmonary systems all undergo deterioration and loss of physiologic reserve with aging. Renal function decreases with age and serum creatinine is a poor surrogate for glomerular filtration rate (GFR) in elderly patients [3]. Renal drug dose adjustment and proper perioperative fluid balance are essential in attempting to minimize morbidity. Cardiac changes that accompany aging include a lower sensitivity to beta adrenergic modulation, altered calcium regulation and an overall reduction in ejection fraction [2]. Occult coronary artery disease is not uncommon and a high index of suspicion for underlying cardiac pathology and prompt preoperative cardiology consultation is essential. A decline in immune function in the elderly has two important implications for the urologic surgeon. First, immune decline may predispose individuals to the development and progression of cancer. Altered immunologic function may also lead to an increased susceptibility to infection during cancer therapy [3]. A significant reduction in liver volume with aging is also

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accompanied by an overall decrease in hepatic function, which can have implications when dosing chemotherapeutic agents. Finally, decreased respiratory function from intrinsic lung disease, weakened respiratory musculature, pulmonary vascular disease, or a combination of the three, can predispose elderly patients to significant postoperative pulmonary complications [2]. Knowledge of these changes with regard to perioperative management is essential in the evaluation of the elderly surgical candidate.

The burden of medical comorbidity frequently impacts clinical decision-making with regard to the pursuit of aggressive oncologic therapy. Comorbidity is also a valuable predictor of perioperative outcomes. Comorbidity scores are useful in the quantification of surgical risk in the elderly. Several useful scores to assess overall comorbidity include the Cumulative Illness Rating Scale for Geriatrics (CIRS-G), the Charlson Comorbidity Index (CCI), and the American Society of Anesthesiologists Classification (ASA). The CIRS-G and CCI have been validated in elderly populations with less favorable scores found to be associated with increased perioperative morbidity and mortality [4, 5]. In fact, overall comorbidity is a more useful predictor of perioperative outcome than chronologic age alone. Sanchez-Sales et al. evaluated outcomes following laparoscopic radical prostatectomy in men ≥70 [6]. In this cohort of 297 men, a CCI ≥2 was associated with a higher risk of short-term postoperative complications compared to those with a lower CCI. Similarly, with regard to laparoscopic renal surgery, Guzzo et al. found a CCI ≥2 to be a significant predictor of perioperative complications in patients ≥75 years of age [7].

Though comorbidity is an important indicator of outcome, it generally does not take into account overall global functioning. Careful preoperative attention to functional status in the elderly surgical candidate can help predict the need for social support and physical rehabilitation services. Functional assessment tools that have been validated in the elderly include the activities of daily living dependency score (ADL) and the instrumental activities of daily living dependency score (IADL). More recently, a comprehensive multidisciplinary tool, the Comprehensive Geriatric Assessment (CGA), has proven effective in both risk stratifying patients prior to intervention and minimizing postoperative morbidity [2]. CGA prior to surgical intervention improves functional status postoperatively and reduces hospital and nursing home stays, thereby decreasing overall medical costs [8].

When the Surgical Task Force at the International Society of Geriatric Oncology designed a survey to identify surgeons' attitudes toward elderly cancer patients, they found that greater than 90 % of surgeons offered surgery regardless of the patient's age. Forty eight percent considered a preoperative frailty assessment mandatory, of which the ASA score, nutritional and performance status were the most frequently used screening tools. CGA was used by only 6.4 % of surgeons in daily practice and only 11.1 % routinely collaborated with geriatricians [9].

Multiple factors often need to be addressed when considering cancer treatment in the geriatric population. The goals of cancer treatment in the elderly include minimizing the impact of treatment on quality of life and maximizing long term functioning and independence. Both physiologic and cognitive changes associated with aging can impact the elderly patient's ability to receive standard oncologic therapies and also may increase the risk associated with various surgical and non-surgical cancer treatments. Functional status, cognition, comorbidity, life expectancy, and risk of functional decline

all must be considered in the elderly cancer patient [10]. Unfortunately, few oncology clinical trials include significant numbers of elderly patients, rendering it difficult to extrapolate standard cancer therapy to this age group. Thus, pre-treatment assessment of the elderly cancer patient's overall health status is imperative.

Prostate Cancer

Introduction

Prostate cancer is the most commonly diagnosed cancer in North American and European men [11]. The National Cancer Institute Surveillance, Epidemiology, and End Results Program (SEER) estimated that 220,800 patients would be diagnosed with prostate cancer in 2015. An estimated 27,540 men would die in 2015, making prostate cancer one of the leading causes of cancer death for men [12]. Despite the significant worldwide burden of the disease, little is known about the etiology of prostate cancer. The incidence of prostate cancer increases with increasing age, documented both clinically and in autopsy studies [11]. The relationship between rising incidence of prostate cancer and age exists both in the U.S. and in Europe [13, 14]. Analysis of the recent SEER database reveals that the median age at diagnosis is 66 years with over 69 % of prostate cancer deaths occurring in men older than 75 years. Indeed, nearly 20 % of new prostate cancer diagnoses occur in men older than 75 years [12]. It is estimated that, by 2030, 20 % of men in the U.S. will be older than 65 years, thereby underscoring the significant public health burden of prostate cancer diagnosis and treatment in the U.S. over the next two decades [15].

Assessment of Comorbidity and Relative Life Expectancy

Given the dramatic impact of PSA screening on prostate cancer diagnosis over the past 20 years, careful consideration must be paid to assessment of patient comorbidity, life expectancy, quality of life, and specific utility functions when deciding whom to screen for prostate cancer. As with any medical decision surrounding whether to treat or not to treat an illness, the risk of disease must be balanced against the risk of treatment, both in terms of survival and health-related quality of life (HRQOL). Prostate cancer is no exception to this rule. The lengthy natural history of the disease and the advanced age at which the disease is frequently diagnosed have raised real questions regarding the need to diagnose (or treat) prostate cancer in patients of advanced age. Management of prostate cancer in the elderly affords clinicians the opportunity to commit two significant errors: "ageism," which refers to denying effective management to someone based strictly upon age, as well as "overtreatment," which refers to the administration of toxic therapies to patients for diseases that, left untreated, are unlikely to result in significant morbidity or mortality [16]. The goal of prostate cancer management in the elderly is to withhold screening and treatment in those whom are unlikely to benefit and to promote screening and treatment in those whom are most likely to benefit.

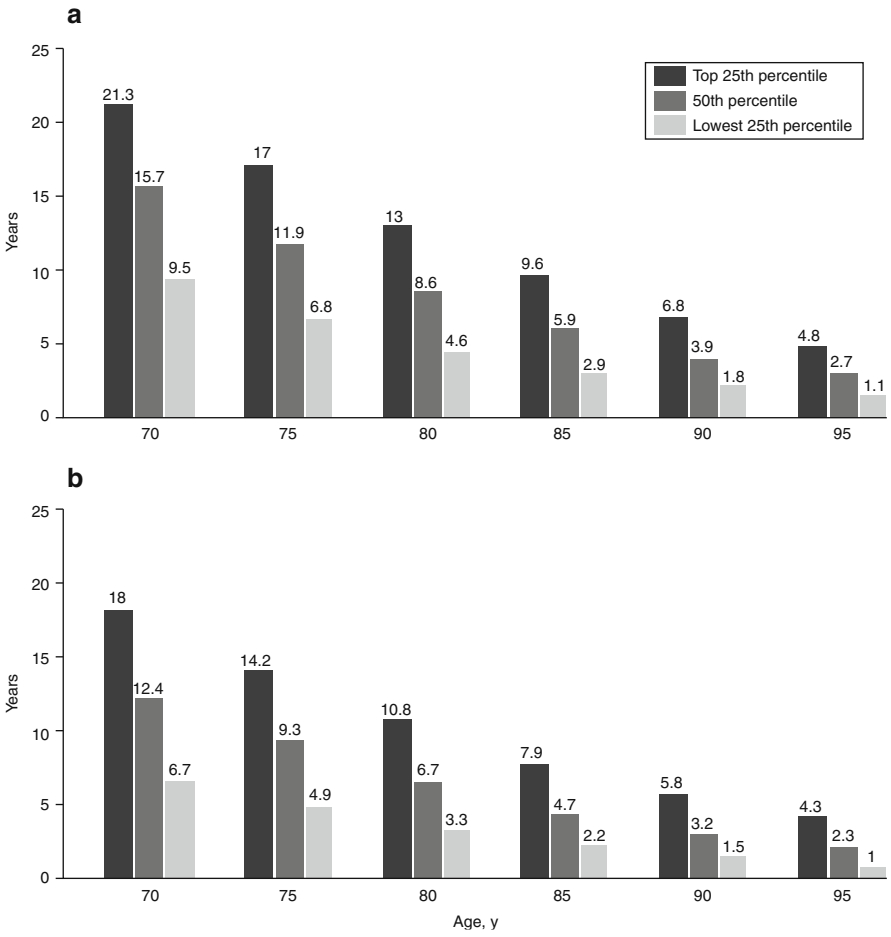

Fig. 7.1 (**a**) Life expectancy for women. (**b**) Life expectancy for men

A patient's remaining life expectancy (RLE) must be incorporated into patient-specific decision-making. Additionally, one must estimate the likelihood that intervention, such as screening or treatment, would benefit the patient within the estimated RLE. Estimation of life expectancy is of utmost importance in an elderly prostate cancer population given the approximately 10-year lead time to associated morbidity and mortality from screen-detected prostate cancers [17]. Therefore, careful attention to life-expectancy tables is helpful when considering prostate cancer treatment. Walter and Covinsky evaluated life expectancy and risk of death from various solid tumors in both men and women. Evaluation of life-expectancy tables reveals that, for a healthy 75 year-old male (top 25th percentile), the patient is expected to live in excess of 14 years. However, for a relatively unhealthy male (bottom 25th percentile), the patient's life expectancy is a mere 4.9 years (Fig. 7.1) [18].

Characteristic	Age at diagnosis							
	66–74 years				75+ years			
	5-years mortality		10-years mortality		5-years mortality		10-years mortality	
	Rate per 100*	95 % CI†	Rate per 100*	95 % CI†	Rate per 100*	95 % CI†	Rate per 100*	95 % CI†
T1c, Gleason 5-7, comorbidity = 0								
Overall mortality	11.7	10.2 to 13.1	28.8	25.3 to 32.6	26.3	24.8 to 28.0	67.1	63.3 to 72.4
Prostate cancer specific mortality	1.6	1.1 to 2.4	4.8	2.8 to 8.4	4.4	3.4 to 5.1	14.0	10.6 to 20.9
T1c, Gleason 5-7, comorbidity = 1								
Overall mortality	25.3	20.7 to 29.5	50.5	41.5 to 59.2	39.4	35.9 to 42.5	76.8	70.5 to 82.9
Prostate cancer specific mortality	1.1	0.0 to 2.7	2.0	0.0 to 5.3	5.1	3.3 to 7.2	9.1	5.5 to 14.4
T1c, Gleason 5-7, comorbidity ≤ 2								
Overall mortality	42.5	36.1 to 48.5	83.1	67.4 to 97.2	48.1	42.7 to 52.7	74.4	63.7 to 84.7
Prostate cancer specific mortality	4.3	1.6 to 8.3	5.3	2.5 to 10.0	4.0	1.7 to 6.5	5.0	2.5 to 8.7
T1c, Gleason 8-10, comorbidity = 0								
Overall mortality	26.4	22.2 to 30.8	55.0	43.9 to 65.9	41.4	38.3 to 44.0	77.0	71.5 to 82.5
Prostate cancer specific mortality	13.6	9.6 to 17.8	25.7	15.9 to 40.6	16.3	13.8 to 19.4	27.5	21.5 to 36.5
T1c, Gleason 8-10, comorbidity = 1								
Overall mortality	30.7	23.7 to 41.0	52.0	38.0 to 77.0	47.2	41.8 to 52.5	92.4	79.3 to 99.7
Prostate cancer specific mortality	11.6	3.0 to 23.4	20.2	4.1 to 46.6	11.2	7.3 to 16.1	23.7	9.5 to 44.7
T1c, Gleason 8-10, comorbidity ≤ 2								
Overall mortality	52.0	42.1 to 64.5	64.3	52.0 to 84.9	65.7	55.9 to 70.1	94.3	87.4 to 100.0
Prostate cancer specific mortality	9.6	2.4 to 19.3	13.7	2.7 to 33.4	12.8	7.3 to 18.9	18.8	9.3 to 36.8

Fig. 7.2 Overall and prostate cancer-specific mortality rates for men by years with localized prostate cancer (T1c) (* The mortality rates were derived by using smoothed cumulative incidence curves as described in the text) († Cls were estimated using a bootstrap with 1000 replications)

Assessment of comorbidity and competing risks permits estimation of overall health status and life expectancy. Unfortunately, current risk stratification models cannot predict with complete accuracy those who would benefit from treatment and those who can safely be managed expectantly. Numerous groups have performed competing-risks analyses to determine the likelihood of prostate cancer death compared to death from other causes. Albertson et al. demonstrated that, for men older than 75 with no comorbidities and intermediate-risk prostate cancer, the risk of all-cause mortality at 10-years is 67.1 % compared to 14.0 % for prostate cancer-specific mortality. Men with two or more comorbidities were found to have a risk of all-cause mortality of 74.4 % compared to prostate cancer-specific mortality of 5.0 % (Fig. 7.2) [19]. Numerous comorbidity indices have been studied in prostate cancer populations with particular attention to identifying those patients at significant risk of death from non-prostate cancer etiologies. Boulos et al. evaluated five comorbidity indices and found that the Chronic Disease Score (CDS), Index of Coexistent Disease (ICED), and the Cumulative Illness Rating Scale (CIRS) outperformed more commonly used methods such as the Charlson Comorbidity Index in the population studied [20]. While clinicians frequently make casual judgment regarding the degree of overall health and patient comorbidity, judicious use of validated comorbidity indices may improve prediction of risk of both prostate cancer-specific and all cause mortality and ultimately improve patient-specific decision-making. As discussed above, however, evaluation of comorbidity must be taken in the context of patient-specific disability, frailty, functional dependence, the presence or absence of geriatric syndromes, and vulnerability [16].

PSA Screening in the Elderly

Since the introduction and widespread implementation of PSA screening in the early 1990s, there has been a significant prostate cancer stage migration, favoring the diagnosis of low-grade, low-stage disease [21]. This stage migration, coupled with the remarkable prevalence of histologically detected prostate cancer at autopsy, has prompted many clinicians and patients, alike, to question the necessity of PSA screening. Two randomized trials reported interim survival results detailing the effectiveness of PSA screening on both overall and prostate cancer-specific mortality. The Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial (PLCO) randomized 76,693 men to yearly prostate cancer screening with PSA and digital rectal examination (DRE) or to usual care. The risk of prostate cancer diagnosis was 116 per 10,000 person-years and 95 per 10,000 person-years in the screening and control groups, respectively. The risk of prostate cancer death was found to be 2.0 per 10,000 person-years and 1.7 per 10,000 person-years in the screening and control groups, respectively, indicating both a very low rate of prostate cancer death and a lack of protection conferred by prostate cancer screening [22]. The PLCO study has been widely criticized due to the high rate of contamination found in the control group, as men in this group received the usual care offered by their primary care physicians. Forty percent of the patients in the control group underwent PSA screening within the first year and, by the sixth year, 52 % underwent PSA screening. The high percentage of patients randomized to the control arm of the study who were screened with PSA testing by year 6 has led many to surmise that, while the survival benefit of PSA screening may indeed be small, this effect is largely attenuated by the high rate of screening in the control arm of the PLCO trial. The European Randomised Study of Screening for Prostate Cancer (ERSPC) randomized 182,000 men between the ages of 50 and 74 years to prostate cancer screening or no prostate cancer screening. Unlike the PLCO study, screening in the European randomized trial occurred, on average, every 4 years. The risk of prostate cancer diagnosis was found to be 8.2 % and 4.8 % in the screening and control arms, respectively. In the overall cohort, prostate cancer screening conferred a 20 % reduction in the risk of prostate cancer-mortality. Excluding noncompliant study participants, the prostate cancer-specific mortality benefit improved to 27 %. Despite these findings, investigators determined that 1410 men would have to be screened and 48 men treated to prevent 1 prostate cancer death, suggesting that screening would result in overdiagnosis [23]. Despite the need to screen and treat a large number of men to prevent few prostate cancer deaths, many believe that longer follow-up will result in a larger observed survival benefit with PSA screening. Modeling the number needed to screen (NNS) and number needed to treat (NNT) in the ERSPC study reveals that, by 12 years of follow-up, the NNS and NNT will be 503 and 18, respectively [24].

Most believe that two major differences between the PLCO and ERSPC studies can explain the disparate findings in the results, namely vastly different rates of PSA screening/contamination of the control groups and the variable rates of PSA "prescreening" amongst study participants. As previously discussed, nearly half of the patients assigned to the control arm of the PLCO study were subject to PSA

screening during the trial, likely leading to the modest increase in prostate cancer detection (17 %) in the screening arm compared to the control arm. The rate of contamination of the ERSPC study was significantly less, and the incremental increase in prostate cancer detection in the screening arm was much higher than in the PCLO study (71 %). Additionally, half of the patients in the PLCO study underwent PSA testing and digital rectal exam (DRE) within 3 years of enrollment, leading many to surmise that the prescreened nature of the control arm of the PCLO study attenuated any meaningful difference in prostate cancer-specific mortality [25].

Given the significant challenge in the interpretation of these large randomized trials, not surprisingly, the appropriate use of PSA screening in older age males remains even less clear. The risk of prostate cancer overdetection increases with increasing age, with PSA testing resulting in an overdetection rate of 27 % at 55 years and 56 % by 75 years [17]. Nonetheless, the likelihood of high-risk prostate cancer increases with age, accounting for 43 % of tumors diagnosed in men older than 75 years as compared to 25 % of tumors diagnosed in men younger than 75 years [26]. Assessment of individual comorbidity and overall health status, in addition to ascertainment of patient-specific attitudes towards screening and treatment, are necessary in order to allow patients to make well-informed decisions surrounding participation in PSA screening.

While no consensus guidelines exist to direct physicians as to when to discontinue prostate cancer screening in older men, the U.S Preventative Services Task Force (USPSTF) has issued their recommendations, as have other societies. The USPSTF position in 2008 was that, in men younger than 75 years of age, there was inadequate evidence to determine whether treatment for prostate cancer found by screening improved health outcomes when compared to patients treated after clinical detection. The task force did recommend, however, against screening for prostate cancer in those 75 years or older [27]. Critics of these USPSTF guidelines argued that patients should be assessed for overall health based upon individual factors and not upon chronological age. Indeed, 78 % of men surveyed at a prostate cancer screening clinic disagreed with the recommendation to discontinue screening at age 75 [28].

The USPSTF then issued an updated recommendation statement after the publication of the PLCO and ERSPC data in 2012. Whereas the 2008 position recommended against PSA-based screening for prostate cancer in men 75 years or older and there was insufficient evidence for recommendations in males younger than 75, the 2012 statement recommended against PSA-based screening regardless of age [29]. This updated statement, therefore, has clinical implications for all men, irrespective of age. The implications may even be more significant for the elderly population. A big concern is that those patients who were previously diagnosed and treated for prostate cancer during the PSA-screening era will now present with advanced disease when they are older.

Given the limitations of the USPSTF recommendations, the most recent American Urological Association guideline on the early detection of prostate cancer, published in 2013, does not recommend routine PSA screening in men 70 years of age or older or in any man with less than a 10–15 year life expectancy, though

does state that men 70 years of age and older who are in excellent health may benefit from such screening [30]. The European Association of Urology recommendation published in 2013 regarding the early detection of prostate cancer states that a baseline serum PSA should be obtained at 40–45 years of age, intervals for early detection of prostate cancer should be adapted to the baseline PSA value, and early detection should be offered to those with life expectancy greater or equal to 10 years [31].

Despite little evidence to support the benefit of PSA screening in elderly populations, the prevalence of screening in the USA population has been high [32]. In fact, some series indicate that the rate of screening is higher in patients over age 70 than in those in their 50s [33]. Nonetheless, some evidence indicates that the rate of PSA testing among men older than 75 years declined after the publication of the U.S. Preventative Services Task Force recommendation in 2008 and has continued to decline since the publication of the PLCO and ERSPC studies [34]. With regards to the impact of the 2012 USPSTF recommendations, urologists ordered significantly more *PCA3* and repeat PSA tests and recommended fewer biopsies at the initial visit, though the fraction of patients ultimately undergoing prostate biopsy remained the same pre and post the recommendation statement. Lower age, higher repeat PSA, and a positive DRE were predictors for patients who underwent prostate biopsy in the pre and post-USPSTF periods, based on multivariate logistic regression analysis [35].

Considering the challenges imposed by PSA screening in the elderly, substantial effort has been directed at identifying very low-risk populations of elderly patients in whom PSA screening can be withheld. A longitudinal cohort study of men undergoing PSA screening revealed that no men between 75 and 80 years of age with a PSA of <3.0 ng/mL died of prostate cancer, potentially identifying a subset of men in which PSA screening could be safely omitted [36].

Treatment of Localized Prostate Cancer

Most prostate cancers currently detected in the U.S. are clinically localized. Although many such men have low- or intermediate-risk disease, a majority seek active treatment [21]. Indeed, recent data suggests that 81.7 % of men older than 75 receive active treatment for newly diagnosed prostate cancer. While a higher proportion of patients with high-risk disease receive active treatment (86.4 %) when compared to those with low-risk disease (72.2 %), this difference is modest [37]. The decision to undergo active treatment for localized prostate cancer in an older man must take into account the likelihood of death from prostate cancer, the risk of symptomatic metastatic disease, and the risk of death from other causes. Observational data suggest that elderly men experience more favorable overall survival when treated for low- and intermediate-risk prostate cancer. Men 65–80 years old who underwent active treatment for prostate cancer have a statistically significant survival advantage compared to men that did not undergo active treatment (HR 0.69, 95 % CI 0.66–0.72), even after controlling for comorbidities and other

confounding variables [38]. A more recent cohort study of 3183 men with nonmetastatic prostate cancer at diagnosis with 14 years of follow up revealed that older men with multiple major comorbid conditions were at high risk for other-cause mortality within 10 years of diagnosis (26, 40, and 71 % 10-year other-cause mortality rates among men with three or more comorbid conditions for men aged 60 years or younger, 61–74 years, and 75 years or older at diagnosis, respectively) [39].

There are numerous risk stratification schemes that help predict outcome following treatment. Specifically, D'Amico et al. evaluated the risk of biochemical recurrence 5-years after definitive therapy for prostate cancer and stratified patients into low-, intermediate-, and high-risk subgroups based on clinical stage, PSA, and Gleason score [40]. Within this risk stratification scheme, low-risk patients were those with clinical stage T1c or T2a disease, PSA ≤10, and Gleason score ≤6. Intermediate-risk patients had clinical stage T2b disease, PSA >10 but ≤20, or Gleason score 7 disease. High-risk patients were those with clinical stage T2c or greater, PSA >20, or Gleason score ≥8. These risk-subgroups provide a framework upon which the clinician can assess global prostate cancer risk. In addition to D'Amico's widely utilized risk-stratification schema, there have been a number of published nomograms evaluating the risk of freedom from progression following radical prostatectomy, brachytherapy, and external beam radiation therapy [41–43]. Additionally, a model was developed that helps predict prostate cancer-specific survival following radical prostatectomy [44]. Combining these tools with previously described methods of assessment of comorbidity and overall health provide patient-specific information upon which to base treatment recommendations.

There are numerous well-described management options for a patient diagnosed with clinically organ confined prostate cancer including radical prostatectomy (RP), external beam radiotherapy (EBRT), brachytherapy, or active surveillance. RP involves surgical removal of the prostate and seminal vesicles, and frequently involves staging pelvic lymphadenectomy. Historically, this procedure was performed using an open surgical approach through a low-midline abdominal incision. Advances in open surgical technique during the 1970s and 1980s resulted in significant improvements in the morbidity associated with RP. Specifically, attention to the dorsal venous complex resulted in a reduction in operative blood loss and novel nerve-sparing techniques improved functional outcomes such as continence and erectile function [45]. More recently, robotic-assisted laparoscopic radical prostatectomy (RALP) has been popularized secondary to potential benefits with regard to decreased blood loss and improved time to convalescence [46]. Despite these improvements, RP has generally not been performed in patients over age 70 due to concern regarding the risk of perioperative mortality in patients of advanced age. The AUA guidelines identify the patient most likely to benefit from RP as having a relatively long life expectancy, no significant surgical risk factors, and a preference for surgery [47, 48]. The European Association of Urology defines RP as standard treatment in patients with stage T1b-T2b, Nx-N0, M0 disease with a life expectancy greater than 10 years. The EAU defines RP as optional in younger patients with T1a disease and a long life expectancy and in patients with limited T3a disease, Gleason score 8 or less, PSA 20 ng/mL or less, and long life-expectancy [48, 49].

Radical prostatectomy, as previously discussed, is performed less often in older patients due to concern over the risk of surgery in this patient population. Trinh et al. performed multivariable analyses on 2109 patients aged 75 years or older, out of 115,554 patients total, who underwent open radical prostatectomy between 1998 and 2007. Elderly age increased homologous blood transfusion rates, intra-operative and postoperative complication rates, and the mortality rate. The study also stratified patients according to annual hospital caseload (AHC) and academic status, noting that intra-operative and postoperative complications were highest at low AHC institutions and non-academic centers [50].

Few series have evaluated functional outcomes from RP in the elderly. Kerr and Zeinke reviewed the Mayo clinic experience of 51 patients older than 75 years who underwent RP and found that two-thirds of elderly patients undergoing RP were without perioperative complication. Nonetheless, elderly patients did have a significantly higher rate of urinary incontinence following RP than their younger counterparts (16% versus 3%) [51]. Data from Begg et al. support the finding that chronological age appears to directly impact the risk of urinary incontinence following radical prostatectomy. The risk of perioperative death, however, was more strongly associated with comorbidity than chronological age [52]. There are also few data that specifically address functional outcomes in elderly men following RALP. Shikanov et al. in their single-institution series, found age to be independently associated with the risk of postoperative continence and potency [53].

While there are few randomized trials which compare treatments for clinically localized prostate cancer, there are randomized data that evaluate differences in prostate cancer-related death amongst patients undergoing RP compared to those randomized to watchful waiting. In the Scandinavian Prostate Cancer Group Study Number 4 (SPCG-4), 695 men with clinically localized prostate cancer were randomized to undergo radical prostatectomy or watchful waiting with initiation of androgen ablation in the context of disease progression. Radical prostatectomy resulted in a relative risk of prostate cancer-related death of 0.56 (95% CI 0.36–0.88) at 10 years and 0.62 (0.44–0.87) at 12 years, corresponding to a number needed to treat (NNT) of 15. Those patients randomized to radical prostatectomy also had more favorable rates of distant metastases, local progression, and overall survival. Nonetheless, in the subgroup of patients older than 65 years, there was no discernable difference in prostate cancer-specific mortality, overall mortality, or the risk of distant metastases [54, 55]. The authors caution that the SPCG-4 study was not powered to detect small survival within subgroups, however these data call into question the routine recommendation of radical therapy for clinically localized prostate cancer in the elderly. The application of a “one size fits all” approach is not advisable considering the heterogeneity of prostate cancer, and as described above, patient-specific risk of prostate cancer death must be balanced against death from other causes.

While the SPCG-4 study failed to reveal any difference in prostate cancer-specific mortality amongst those patients older than 65 years treated with RP or watchful waiting, there are data to suggest that elderly patients with high-risk disease benefit from the addition of EBRT to androgen ablation. The SPCG-7/SFUO-3

study randomized patients with high-risk prostate cancer to receive androgen ablation or androgen ablation plus EBRT. At a median of 10.8 years of follow up, those patients who received radiotherapy were found to have a relative risk of death from prostate cancer of 0.44 (95 % CI 0.33–0.66). The magnitude of absolute risk reduction was higher in those patients older than 67 years when compared to those younger than 67 years (12.9 % vs. 9.8 %, respectively) [56]. It is clear that some patients stand to benefit from definitive therapy for prostate cancer and some patients do not. The most significant challenge in treating elderly patients with prostate cancer is attempting to determine whether an individual patient is part of the former or the latter.

EBRT remains a mainstay of treatment for clinically localized prostate cancer in the elderly. The AUA guidelines identify the patient most likely to benefit from EBRT as having a relatively long life expectancy, no significant risk factors for radiation toxicity, and a preference for EBRT [47, 48]. Additionally, the EAU guidelines recommend that the treatment decision should be based upon TNM classification, Gleason score, baseline PSA, age, comorbidity, life expectancy, and health related quality of life (HRQOL). Specific recommendations include the use of 3D-conformal radiation therapy (CRT) with or without intensity modulated radiation therapy (IMRT) for patients with T1c-T2c N0 M0 disease with dose escalation for those patients with intermediate-risk disease (T2b, PSA 10–20, Gleason score 7) [48, 49].

The question of whether one should be treated for prostate cancer revolves largely around the patient's burden of comorbid disease and desire for treatment. Generally, the rates of biochemical control and cancer-specific survival are similar when comparing external beam radiotherapy and radical prostatectomy [57, 58]. As such, many practitioners who treat prostate cancer will base treatment recommendations upon a specific patient's utility function(s). As previously described, there has been a tendency amongst practitioners who treat prostate cancer to not recommend surgery in patients older than 70 years secondary to increasing risks of perioperative morbidity. External beam radiotherapy is feasible in patients of advanced age, however unlike radical prostatectomy, there are no randomized trials comparing radiation therapy to expectant management. Fiorica et al. evaluated their experience with radiotherapy for local and locally advanced prostate cancer in patients greater than 75 years. The authors determined that patients' burden of comorbid illness (as measured by the adult co-morbidity evaluation index) was inversely related to overall survival. However, overall survival was not affected by receipt of external beam radiation therapy. While comorbidity was found to strongly associate with the risk of acute bowel and urinary toxicity, there was no documented relationship between chronological age and acute or late toxicity [59]. This underscores the points raised previously in this chapter relating to the importance of careful assessment of patient comorbidity in the evaluation of both need for treatment and specific treatment choice. These data are consistent with previously published reports from pooled EORTC studies. Pignon et al. evaluated 1619 patients who underwent radiotherapy for pelvic malignancy and determined that age was not associated with increasing radiation toxicity, thereby leading the investigators to conclude that

chronologic age is not a limiting factor for radiotherapy for pelvic malignancy [60]. These findings have been confirmed by a number of groups in a number of practice settings leading many to conclude that radiotherapy is a reasonable treatment option for men with localized or locally advanced prostate cancer [61–63].

In addition to external beam radiotherapy, brachytherapy is a reasonable therapeutic option for men with localized low-risk disease. Unlike external beam radiation, brachytherapy is typically reserved for men with low-grade (Gleason score 6 or less) disease, minimal lower urinary tract symptoms, and small to moderate prostate volume (<50 g). In appropriately selected patients, brachytherapy achieves excellent rates of biochemical progression free survival, with cure rates approaching 99 % in low-risk populations [64]. When compared to radical prostatectomy, patients undergoing brachytherapy tolerate the procedure quite well with favorable long-term quality of life outcomes [65]. Nonetheless, there are a number of problems with the general application of brachytherapy to the elderly population. Given the morbidity with regard to urinary function in men who undergo interstitial brachytherapy, many practitioners will not perform the procedure as primary prostate cancer treatment in men with significant pre-treatment urinary bother (IPSS > 15). Indeed, both pre-treatment IPSS and prostate volume are strong predictors of post-treatment urinary toxicity in patients undergoing brachytherapy [66, 67]. Given the high prevalence of BPH and lower urinary tract symptoms in elderly men, there is considerable (and appropriate) concern over the long-term urinary morbidity of brachytherapy, which limits its general application. Furthermore, given the low-risk nature of most tumors treated by brachytherapy, there is significant debate over whether or not any therapy (brachytherapy or otherwise) is indicated in elderly men with low-risk disease. Thus, while brachytherapy remains a treatment option for men with localized prostate cancer, it has not received wide acceptance in the elderly.

With the introduction and widespread dissemination of PSA screening in the early 1990s came a remarkable stage migration in prostate cancer epidemiology favoring the diagnosis of low-risk disease [21]. As discussed previously, this stage migration has generated a considerable amount of concern surrounding the overtreatment of clinically insignificant prostate tumors. Despite the nominal risk of prostate cancer-specific mortality in men diagnosed with low-risk disease, more than 90 % of such men receive definitive treatment, typically in the form of surgery or radiation therapy [68]. Given the competing risks of overall mortality in the cohort of patients diagnosed with prostate cancer in contemporary series, there has been growing interest in active surveillance with curative intent, a paradigm by which patients are monitored until they demonstrate evidence of disease progression at which time definitive therapy is triggered. Active surveillance is dissimilar from watchful waiting, a paradigm by which patients are treated only should they develop symptoms often attributable to metastatic disease. Among the theoretical benefits of active surveillance is a significant reduction in prostate cancer overtreatment, particularly in elderly men who stand to benefit little from radical therapy.

Active surveillance series are beginning to mature and show promising results. Enrollment criteria for the Johns Hopkins Active Surveillance program includes

patients with clinical stage T1c disease, PSA density less than 0.15 ng/mL, Gleason score 6 or less, two or fewer biopsy cores with cancer, and a maximum of 50 % involvement of any core with cancer [69]. The report published in 2011 included a total of 769 men with a median follow up of 2.5 years and found that a total of 33 % of men underwent intervention at a median time of 2.2 years with 73.7 % of these men doing so for biopsy reclassification. Nonetheless, there were no men in the Johns Hopkins Program who developed distant metastatic disease or died from prostate cancer [70]. In 2015, the intermediate and longer-term outcomes from a prospective active surveillance trial for favorable-risk (i.e., very low risk or low risk) prostate cancer was published. This study included 1298 men with a median follow up of 5 years. Overall, cancer-specific, and metastasis-free survival were 93 %, 99.9 %, and 99.4 % at 10 years, respectively, and 69 %, 99.9 %, and 99.4 % at 15 years, respectively. Notably, patients included in the study were those that met the initial Johns Hopkins Active Surveillance program criteria previously described, as well as older men with low-risk disease (i.e., clinical stage≤T2a, PSA <10 ng/mL, and Gleason score ≤6). Nine hundred twenty six men (71 %) met all of the very low risk criteria and 372 (29 %) met criteria for low risk cancer [71]. Another active surveillance cohort is from the University of Toronto, where the surveillance cohort is somewhat more heterogeneous. Enrollment criteria in the Toronto program includes all low-risk patients (Gleason score 6 or less and PSA less than 10 ng/mL); however, from 1995 to 1999 the program did enroll patients older than 70 years with PSA up to 15 ng/mL or Gleason 3+4 disease. Investigators followed 450 patients for a median of 6.8 years and reported a treatment rate of 30 %. The 5- and 10-year cancer-specific survival in the cohort was 99.7 % and 97.2 %, respectively, with a hazard ratio for other-cause mortality of 18.6 (95 % CI 7.6–45.7) [72].

Researchers from The Netherlands sought to estimate the individual benefit of immediate treatment or active surveillance for prostate cancer after screen-detection in men 66–72 years of age by using a microsimulation model of the natural history of prostate cancer and individual life histories using US comorbidity lifetables based on a random sample of MEDICARE data. For men with low risk disease (≤T2a, Gleason 6) undergoing immediate treatment (i.e., radical prostatectomy or radiation therapy), the probability of overtreatment was 61–86 %, which decreased to 37–46 % if assigned to active surveillance. Overtreatment ranged from 23 to 60 % for intermediate risk men (≤T2, Gleason 3+4) undergoing immediate treatment, which decreased to 16–31 % if assigned to active surveillance. Lastly, overtreatment ranged from 11 to 51 % for high risk men (T3 or≥Gleason 4+3) who underwent immediate treatment. The study concluded that active surveillance significantly reduced overtreatment at a modest cost for low risk men, that immediate treatment versus active surveillance for intermediate risk men should be based on age and comorbidity status, and that men with high risk disease may benefit from immediate treatment even after 69 years of age [73].

While the risk of prostate cancer-specific mortality seems low compared to other competing causes of death, particularly in patients with a moderate to high burden of medical comorbidity, there remains some concern about missed opportunity for intervention. Warlick et al. evaluated the risk of “noncurable”

cancer in patients undergoing immediate radical prostatectomy compared to delayed surgery after having been enrolled in an active surveillance program. Using a definition of "noncurable" cancer as adverse pathology associated with a less than 75 % chance of remaining disease-free 10 years after surgery, the investigators found that, after adjustment for PSA density and age, there was no difference in the risk of "noncurable" cancer between those treated immediately and those undergoing delayed intervention [74]. These data indicate that there is little risk in enrollment in active surveillance with delayed intervention. There remains some controversy, however, regarding the safety of delayed treatment. O'Brien et al. evaluated patients with D'Amico low-risk disease and determined that those patients who suffered a treatment delay of 6 months or greater were found to have higher risk of pathologic upgrading and biochemical failure after prostatectomy. Surgical delay remained an independent predictor of biochemical failure on multivariable analysis when controlling for PSA and clinical stage [75]. Thus, while active surveillance appears to be a safe management strategy for many men with low-risk prostate cancer, long-term follow up will be required to carefully assess the survival implications associated with delayed intervention. The elderly population, particularly elderly patients with low-risk disease, should certainly be counseled regarding the merits and pitfalls of active surveillance.

The International Society of Geriatric Oncology (SIOG) published recommendations for the assessment and treatment of prostate cancer in older men. Based on a systematic evaluation of comorbidities, dependence status, and nutritional status, older men with prostate cancer can be classified into one of four health status categories which, rather than chronological age, should be used when considering treatment options for localized and advanced prostate cancer: The 'healthy' or 'fit' patient has no serious comorbidities, is functionally independent, and has no malnutrition and, therefore, is considered to be able to tolerate any form of standard cancer therapy. The 'vulnerable' patient is dependent in one or more instrumental activities of daily living but no dependence on activities of daily living, has one comorbid uncontrolled condition, or is at risk of malnutrition. These patients might benefit from geriatric intervention and, after resolution of their geriatric problem, can receive standard cancer therapy. The 'frail' patient is dependent in one or more activities of daily living, has two or more uncontrolled comorbid conditions, or has severe malnutrition. These patients should benefit from geriatric intervention and their cancer treatment should be adapted to them. Lastly, the 'too sick' patient has a very poor health status and is likely to be suitable for palliative end-of-life treatment only [48].

The diagnosis and management of elderly patients with prostate cancer remains a challenge to treating physicians. Unlike many other malignancies, the risk of diagnosis and treatment must be carefully considered in the context of competing risks of death. Working groups have begun to develop paradigms for prostate cancer management in the elderly (Fig. 7.3). Utilization of prediction tools coupled with the use of such management paradigms will help clinicians and patients alike achieve optimal treatment strategies. While current prediction tools remain imper-

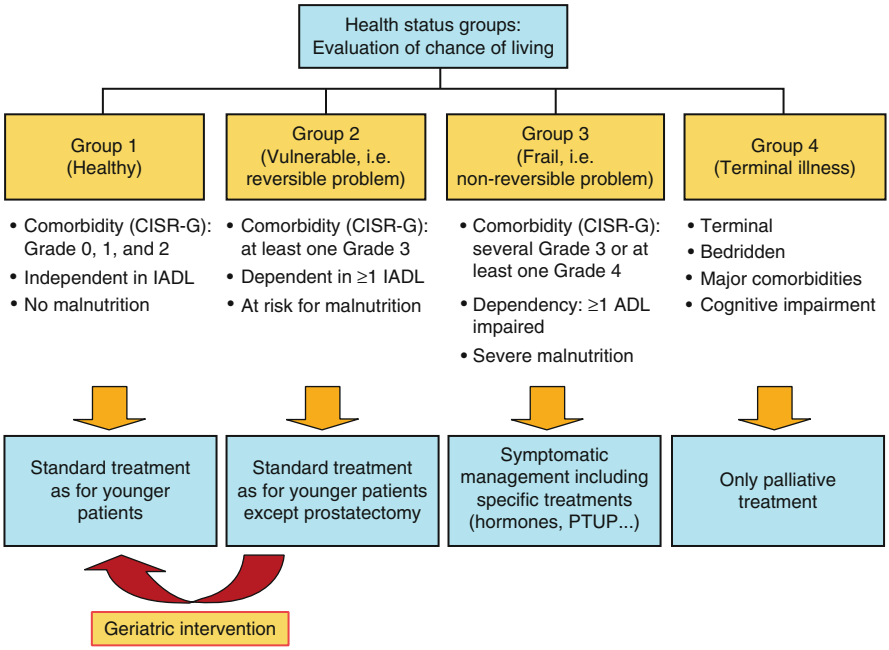

Fig. 7.3 A decision tree for treating patients with: (**a**), localized disease; and (**b**), metastatic disease

fect, they are helpful in the quantification of risk when counseling such patients. As data from ongoing studies begins to mature, we will continually have to reassess the paradigm of prostate cancer screening, diagnosis, and treatment.

Bladder Cancer

Introduction and Epidemiology

Bladder cancer is a commonly diagnosed malignancy in both men and women, accounting for an estimated 74,000 incident cases and 16,000 deaths in 2015. Like many other malignancies, bladder cancer occurs most commonly in the elderly, with the median age at diagnosis being 73 years and the median age of death 79 years [12]. The incidence of bladder cancer seems to increase with increasing age. Schultzel et al. evaluated the California Cancer Registry and determined that the incidence of bladder cancer peaks in those patients 85 years and older, regardless of sex or ethnic background. Interestingly, these investigators documented a 10 year difference in peak incidence between lung/bronchus cancer and bladder cancer despite similar risk factors such as smoking and occupational exposure [76]. Nonetheless, there is a strong association of bladder cancer incidence with age, with an overall incidence of 27.3 % in patients under 65 years and 72.7 % in those over 65 years [12].

Bladder cancer treatment and outcome is largely determined by disease grade and stage. While nonmuscle-invasive tumors are frequently managed with transurethral resection and intravesical immunotherapy/chemotherapy, muscle-invasive tumors require radical therapy traditionally in the form of radical cystectomy and urinary diversion. Given the significant difference in treatment strategy amongst patients with either nonmuscle-invasive or muscle-invasive disease, there is considerable interest in identifying relationships that exist between chronologic age and disease aggressiveness. It seems there is a direct relationship between age and the risk of diagnosis of muscle-invasive disease. Konety et al. using SEER data, found that the risk of muscle-invasive bladder cancer increases to 32.4 % in patients 85 years or older from 23.8 % in those 55 to 64 years [77, 78]. This relationship was confirmed by Prout et al. who, using similar data, found the risk of muscle-invasive disease to be 28.7 % in patients 85 years or older compared to 19.4 % in those less than 55 years [78, 79].

Nonmuscle-Invasive Bladder Cancer: Treatment Implications in the Elderly

The hallmarks of treatment for nonmuscle-invasive bladder cancer are transurethral resection and intravesical immunotherapy/chemotherapy. In the group of elderly patients with nonmuscle-invasive disease, endoscopic procedures, including transurethral resection, are generally well tolerated. Transurethral resection rarely creates scenarios in which major fluid shifts or pressures are transmitted to the cardiopulmonary, renal, or hepatic systems. [3] Generally, patients with low-grade, nonmuscle-invasive disease face little risk with regard to disease progression. Specifically, the risk of progression in patients with low-grade Ta disease is approximately 5–10 %. Emphasis is placed on local disease control, with particular attention paid to limiting the morbidity associated with such tumors. Patients with high-grade tumor(s), invasive disease, or carcinoma-in-situ, however, face higher risk of disease progression ranging from 15 to >50 % depending on the specific stage and grade of the tumor [80]. Traditionally, transurethral resection, in combination with intravesical immunotherapy and/or chemotherapy, has been used to reduce both disease recurrence and progression. Bacillus Calmette-Guerin (BCG) is the most common form of intravesical therapy used in the United States. Intravesical administration of BCG results in a local immune response with cytokine induction favoring interferon-γ and IL-2. Such response is thought to activate cell-mediated cytotoxic mechanisms that translate into the observed reduction in disease recurrence and progression [80, 81].

The efficacy of intravesical BCG in reducing the likelihood of disease recurrence and progression has been well described in the literature [80, 82–86]. Nonetheless, there is a growing body of evidence to suggest that the response to BCG is attenuated in the elderly. Joudi et al. evaluated data from a national phase II multicenter study of BCG plus interferon-alpha to assess differences in response to treatment based upon age. Investigators found the 2-year recurrence-free survival

rates in patients 80 or older and 61–70 years to be 39 % and 61 %, respectively. The response rates amongst elderly patients were lower than younger patients regardless of whether these patients were BCG-naïve or had been previously treated [87, 88]. Herr et al. reviewed the Memorial Sloan Kettering experience and found that, while there was no difference in recurrence-free survival at 2 years, after 5 years, those patients older than 70 years demonstrated less favorable recurrence-free survival when compared to those younger than 70 years (27 % versus 37 %, respectively) [89]. It is known that both innate and adaptive immunity declines with age and as such, it is theorized that elderly patients may not be able to mount the immune response necessary for optimal BCG response [3, 90]. Nonetheless, the magnitude of age as a negative predictor of response to intravesical BCG likely remains fairly small.

While the response to BCG appears to be somewhat attenuated with advancing age, there is some evidence to suggest that morbidity from treatment increases with advancing age. Heiner et al. reviewed their experience of men receiving maintenance BCG and found the complication rate for patients less than 70 years and greater than 70 years to be 17.6 % and 48.6 %, respectively. The most common complications reported in this series included cystitis/bladder pain severe enough to discontinue therapy, chills/fever, and severe prostatitis/epididymitis. These data led the authors to conclude that maintenance should be given with caution in men over age 70 and should be avoided in patients over age 80 [91]. There are few other series that specifically address the risk of complication from intravesical BCG in the elderly; however, there are a number of case reports that raise concern over this association [87, 92, 93]. Clearly, the benefits of intravesical BCG with regard to reduction in the risk of disease recurrence and progression must be weighed against the risks of BCG therapy in patients of advanced age.

Muscle-Invasive Bladder Cancer: Treatment Implications in the Elderly

The gold standard treatment for muscle-invasive bladder cancer is radical cystectomy (RC) and urinary diversion [94]. Furthermore, recent data supports the use of neoadjuvant platinum-based chemotherapy in patients with muscle-invasive bladder cancer [95–97]. Nonetheless, radical surgery and systemic chemotherapy confer significant “stress” to a number of organ systems, and given the gradual decline in physiologic capacity among the elderly, each of these interventions is limited by the patients’ abilities to tolerate the insult(s) of treatment [3]. Patients aged 75 years or older have, not surprisingly, a higher prevalence of cardiac disease, prior cancer diagnosis, chronic anemia, and less favorable American Society of Anesthesiologists (ASA) Classification than those less than 75 years [79].

The substantial burden of comorbidity in patients of advanced age has resulted in dramatic variations in care amongst elderly patients with muscle-invasive bladder cancer. Prout et al. using SEER data, noted that patients over 80 years old were far less likely to receive RC than their younger counterparts (16 % versus 40–55 %, respectively) [79]. These data were confirmed by Konety et al. who demonstrated

that the likelihood of undergoing RC was lower in patients older than 75 years than patients younger than 75 years and by Schrag et al. who demonstrated that patients older than 85 years had an adjusted odds ratio of undergoing cystectomy of 0.11 (95 % CI 0.09–0.15) when compared to those 65–69 years old [77, 98]. Hollenbeck et al. reported a cystectomy rate of 11.5 % in patients older than 80 years with muscle-invasive bladder cancer. Nonetheless, radical/partial cystectomy resulted in the greatest risk reduction in both bladder cancer-specific and overall mortality [99]. The exact nature of the bias for or against RC in the elderly is unknown, but possible reasons include delay in diagnosis, the inappropriate use of less aggressive therapy, or the perception that older patients would not tolerate a major operative procedure [4].

Variation in bladder cancer care amongst the elderly is not limited, however, to rates of surgical extirpation. Porter et al. evaluated the use of systemic chemotherapy for bladder cancer and demonstrated that age was indirectly associated with the likelihood of receiving such treatment [100]. Reardon et al. recently looked at the trends in the use of perioperative chemotherapy and 5692 patients met the study's inclusion criteria. Neoadjuvant chemotherapy use increased significantly from 2006 to 2010, though adjuvant chemotherapy remained stable. Multivariable modeling revealed that advanced age, among other factors, was negatively associated with receipt of perioperative chemotherapy [101].

Even though elderly patients may have diminished functional reserve related to either advanced cancer or chronologic age making delivery of cytotoxic chemotherapy particularly challenging, chemotherapy should still be considered as part of the therapy [102]. A recent study assessed the clinical outcomes following neoadjuvant cisplatin-based chemotherapy for bladder cancer in the elderly versus those in younger patients and found that overall survival, relapse-free survival, rates going forward to definitive local therapy, pathological complete response rate, and disease relapse rate were similar between those ≥70 years of age and those <70. The study concluded that elderly patients with good functional status and few comorbidities with muscle invasive bladder cancer have similar clinical outcomes as their younger counterparts after undergoing neoadjuvant chemotherapy followed by definitive cystectomy or radiotherapy [103].

Nonetheless, there are a number of questions as to why utilization of systemic chemotherapy in patients with muscle-invasive bladder cancer remains so poor. Certainly renal function compromise can result in reduced ability to administer chemotherapy, however, underutilization exists even in patients with acceptable renal function [104]. As with the variation in cystectomy rates, the reasons for such profound underutilization of systemic chemotherapy are likely multi-factorial. More work must be done to identify barriers to improve the quality of care delivered to elderly patients with high-risk muscle-invasive bladder cancer.

Consideration of outcomes following RC in the elderly is challenging given the retrospective nature of many of the published case series, the varied definition of "elderly," and the failure amongst investigators to adequately evaluate comorbid disease and functional capacity. Indeed, the use of chronological age, as previously described, is far less informative than the careful assessment of comorbidity,

functional capacity, and disability, particularly when considering major abdominal surgery in an elderly population. Chamie et al. using SEER data, demonstrated a survival advantage associated with RC in all age groups with the exception of octogenarians, who demonstrated only a 3 month overall survival benefit (18 months versus 15 months) which improved when those with nodal or metastatic disease were excluded (23 months versus 15 months) [105]. Fairey et al. found that chronological age was not associated with the risk of 90-day mortality or early postoperative complications, however, that comorbodity was a strong predictor of 90-day mortality and early postoperative complications [106]. Contrary to these findings, Liberman et al. demonstrated that both septuagenarian and octogenarian age increased the risk of 90-day mortality after RC [107]. Konety et al. found that increasing age was independently associated with in-hospital mortality after RC and Hollenbeck et al. reported that increasing age was associated with increasing risk of postoperative complication after RC [108, 109]. Koppie et al. incorporated age-adjusted Charlson comorbidity index (ACCI) into their evaluation of RC outcomes and determined that increasing ACCI was associated with increasing risk of pT3+ disease, decreasing likelihood of lymphadenectomy, and decreasing likelihood of postoperative chemotherapy. Furthermore, higher ACCI was associated with worse overall but similar recurrence-free survival [110]. Siegrist et al. evaluated the Memorial Sloan Kettering experience and found that octogenarians experienced a nonsignificantly higher rate of minor (55 % vs. 51 %) and major (17 % vs. 13 %) complications compared to younger patients within 90 days of surgery, however, octogenarians were more likely to die within 90 days of surgery (6.8 % vs. 2.2 %, $p = 0.01$). Interestingly, while octogenarians were more likely to die of non-bladder cancer related causes, bladder cancer-specific survival was similar between octogenarians and younger patients [111]. It is difficult to identify the reasons for differences between studies. While some series indicate that chronological age does afford some predictive value when it comes to the risk of complication or early mortality, some fail to demonstrate this relationship. The decision to proceed with radical surgery should be individualized to allow for adequate consideration of chronologic age, comorbidity, and functional status. Doing so will permit the most comprehensive evaluation of individual risk and potential benefit from radical surgery. As RC has a demonstrable benefit in the geriatric population, chronologic age alone should not be used to exclude patients from surgery. In patients who are either unfit or unwilling to undergo RC, bladder sparing protocols in the form of systemic chemotherapy, external beam radiation, and aggressive transurethral resection may present a viable option [112]. However, bladder sparing protocols may be less likely to provide a cure, may adversely affect long term quality of life, have significant side effects, and may only provide short-term palliation [113].

Noncontinent diversion in the form of an ileal conduit is the most common urinary diversion employed in elderly patients following RC [114]. Though continent diversion in the form of an orthotopic neobladder or a cutaneous catheterizable reservoir offer the advantage of continence without the need for an external appliance, there is significant concern over the increased risk of complication in the elderly population [115, 116]. Recent data, however, suggest that radical cystectomy

and urinary diversion, including orthotopic bladder substitution, can lead to good oncological and functional outcomes in older patients. In patients older than 75 years of age who underwent open radical cystectomy with urinary diversion from 2000 to 2013, with a median age of 79.2 years, the 90-day complication rate was 54.3%, 56.7%, and 63.6% in the ileal orthotopic bladder substitute (OBS), ileal conduit (IC), and ureterocutaneostomy (UCST) groups, respectively. The 90-day mortality was 0%, 13%, and 10% in the OBS, IC, and UCST groups, respectively. Overall and cancer-specific survivals were 90 and 98 months for the OBS group, 47 and 91 months for the IC group, and 11 and 12 months for the UCST group, respectively. Outcomes were better for those who underwent OBS likely because those with MIBC who underwent OBS had significantly lower pT stages compared to patients in the other groups [117]. Even though the patient's baseline cancer characteristics were not similar between the three groups, this study suggests that some elderly patients may be good candidates for continent diversions.

Concerns have been raised over functional outcomes following continent diversion in the elderly, however. Madersbacher et al. evaluated functional outcomes following orthotopic neobladder and determined that increasing age was associated with lower reservoir capacity, increased nocturia, and increased rates of day and nighttime incontinence [118]. Hautmann et al. confirmed these findings, reporting an increased risk of incontinence in elderly patients undergoing orthotopic neobladder [118, 119].

Lastly, Winters et al. also studied radical cystectomy in elderly patients, though compared the robotic versus open technique. There were no significant differences in baseline comorbidities, clinical or pathologic stage, or use of neoadjuvant chemotherapy between groups and mean number of lymph nodes removed were similar. Mean operating room times for the robotic group were significantly longer, though robotic surgery was associated with less blood loss and a shorter length of stay compared to the open approach. Surgical complication and 90-day readmission rates were similar between the two groups [120]. Therefore, recent data suggests that elderly patients may not only be acceptable candidates for radical cystectomy, but that they may be acceptable candidates for more complex surgery, such as orthotopic urinary diversion, and less invasive surgery, such as with the robotic-assisted approach.

Kidney Cancer

Introduction and Epidemiology

Renal cell carcinoma (RCC) remains a common malignancy among the elderly with over 58,000 new cases diagnosed in 2010 and over 13,000 deaths attributed to the disease during the same time period [13]. The SEER data groups kidney and renal pelvic cancer together, in which case they accounted for an estimated 61,560 new cases in 2015 and 14,080 deaths in the same year [12]. Furthermore, the

incidence of RCC continues to rise in the United States with diagnosis rates of localized tumors outpacing that of advanced or metastatic disease [121, 122]. Many attribute the observed increase in diagnosis of localized RCC to the more liberal application of imaging techniques. Between 13 and 27 % of abdominal imaging studies identify a renal lesion, the majority of which are benign cysts that require no treatment [123, 124]. The largest increase in incidence of small renal masses has been observed in those patients older than 70 years, possibly owing to the frequent use of imaging in the elderly [125]. Historically, patients with RCC presented with the classic triad of hematuria, flank pain, and flank mass, however, in contemporary series, the majority of new renal masses are diagnosed incidentally on imaging studies performed for non-renal indications [126, 127].

Kidney cancer is largely a disease of the elderly with the median age at diagnosis of 65 years with 25 % of newly diagnosed patients older than 75 years [128]. As with other genitourinary malignancies, there are multiple considerations that must be taken into account when treating elderly patients with newly diagnosed RCC. There are conflicting data surrounding the implication(s) of age on clinicopathologic features at RCC diagnosis. Verhoest et al. evaluated 4774 patients from various European centers and found that increasing age was associated with increasing tumor size and nuclear grade. Furthermore, increasing age was inversely associated with cancer-specific and overall survival [129]. Despite advances in cross-sectional imaging, nearly 20 % of suspicious renal masses are benign at pathologic analysis [130]. Recent attention has been paid to active surveillance of small, incidentally detected renal masses. Kouba et al. observed 46 patients with small renal masses and found that the tumor growth rate was slower in patients over 60 years when compared to their younger counterparts (0.6 cm versus 0.9 cm, respectively) [125]. Unfortunately, the relationship between age and RCC-specific outcome is poorly characterized and warrants further investigation.

As with other tumor types, considerable attention has been paid to the development of prognostic models for cancer-specific and overall mortality in an attempt to define competing risks. These methods are particularly applicable in the elderly given the slow growth-rate and low metastatic potential of small renal masses (<3 cm) [131]. Karakiewicz et al. developed a nomogram to predict 1, 2, 5, and 10-year RCC-specific survival. The model incorporates age, gender, the presence of symptoms, tumor size, T-stage, and the presence of metastatic disease and, in an external validation cohort, demonstrated excellent accuracy [132]. More recently, Kutikov et al. using a SEER cohort, found the overall risk of RCC-related death, other cancer death, and non-cancer death to be 4 %, 7 %, and 11 %, respectively [133]. The investigators developed nomograms to predict the risk of death from RCC, risk of death from other cancer, and risk of non-cancer death which are particularly useful when counseling patients with a small renal mass and significant risk of perioperative morbidity. As with prostate and bladder cancer, it is critically important to incorporate validated prediction tools into everyday clinical practice. Doing so will allow patients to make informed, careful decisions about their care.

Treatment of Localized RCC in the Elderly

The last decade has brought significant change to the paradigm of treatment for localized RCC. Historically, the gold standard of treatment for localized RCC was radical nephrectomy (RN) as described by Charles Robson [134]. However, growing concern over the risk of chronic kidney disease (CKD) secondary to radical nephrectomy has resulted in considerable interest in renal preservation in the form of nephron sparing surgery (NSS), ablative techniques, and active surveillance (AS). Prior to undertaking any form of therapy for localized RCC, careful attention must be paid to global renal function. Serum creatinine is not an accurate surrogate for overall renal function in the elderly, and as such, glomerular filtration rate (GFR) should be estimated using a standardized equation such as the Modification of Diet in Renal Disease (MDRD) or performing a 24 h urine creatinine clearance [135]. Canter et al. evaluated the prevalence of baseline CKD in patients presenting to a referral cancer center with a solid renal tumor and found that 40 % of patients 70 years or older had CKD stage III (GFR 30–60). Furthermore, 23 % of patients older than 70 years had CKD stage III with a "normal" baseline serum creatinine (≤1.4 mg/dL) underscoring the need for GFR calculation in the elderly [136].

Attention to the presence of CKD is important because there is a well-documented relationship between CKD and the risk of death, cardiovascular events, and hospitalization [137, 138]. Furthermore, there is a growing body of evidence surrounding the incremental risk of CKD associated with undergoing radical nephrectomy when compared to partial nephrectomy (PN). Huang et al. determined that patients undergoing RN were significantly more likely to suffer from stage III or greater CKD than those undergoing PN [139]. Furthermore, Thompson et al. evaluated the Mayo Clinic experience and identified patients treated with radical or partial nephrectomy for a solitary small renal mass and found that RN was associated with increased risk of death despite adjustment for known confounders and comorbidity leading investigators to postulate that the observed increase in the risk of death may be attributed to increased risk of cardiovascular disease [140]. Taken together, these data suggest that the risk of CKD following RN is significant, and given the known relationships between CKD and cardiovascular disease, efforts should be made to preserve renal function [141].

Surgical excision remains the gold standard for localized renal cell carcinoma. While efforts should be made to preserve renal function, there remain circumstances in which NSS is not technically possible. As such, RN remains a therapeutic option for a patient with localized RCC in the most recent AUA guidelines [142]. Indeed, RN can be performed with acceptable morbidity in the elderly. Specifically, numerous series have evaluated the incremental morbidity associated with undergoing RN at advanced age and have not documented any increase in perioperative morbidity or mortality [143, 144]. There is increasing evidence that NSS affords patients comparable recurrence-free and long-term survival rates when compared to patients undergoing RN [141, 145]. Given the renal functional advantages afforded by NSS in the context of equivalent oncologic outcomes, the AUA guidelines do encourage physicians to counsel patients about the potential advantages of a nephron-sparing

treatment approach in both the imperative and elective settings [142]. Furthermore, though NSS was historically performed for obligate indications, recent years have seen a profound expansion in utilization of NSS for larger, more complex, tumors. Longer follow-up will be required to determine whether the protective effects of renal preservation outweigh the potential oncologic risks incurred by these expanded indications.

The robotic-assisted approach, as with prostate and bladder cancer, has made its way into the treatment algorithm for renal cell. In a retrospective study of consecutive patients undergoing robotic-assisted partial nephrectomy from 2006 to 2010, 37 patients ≥70 years were matched with patients <70 years and tumor characteristics, renal function, nephrometry score, incidence of renal cancer in lesions, ASA scores 1–4, and Charlson Comorbidity Index scores were similar between the two groups. There was no difference in perioperative and postoperative outcomes between the two groups, suggesting that the robotic-assisted approach for small renal masses may be a safe alternative for patients >70 years of age [146].

In addition to surgical extirpation, there has been increasing interest in the use of ablative techniques in the treatment of localized RCC. Currently the two most common techniques include cryoablation and radiofrequency ablation (RFA). Either energy can be delivered percutaneously or laparoscopically. Given the relatively lower risk of major urological complication with the use of ablation when compared to open or laparoscopic partial nephrectomy there has been considerable interest in applying this technique to elderly patients [142]. Choueiri et al. found that, on multivariable adjusted analysis, age was directly associated with the likelihood of undergoing ablation for a small renal mass. The same study failed to demonstrate any difference in cancer-specific or overall survival between ablation and surgical extirpation [147]. Kunkle et al. performed a meta analysis to evaluate the efficacy of various treatments for localized RCC and found that patients undergoing ablative techniques suffered from a higher risk of local recurrence, however, the investigators did not document any difference in metastatic progression [148]. Unfortunately, the comparative effectiveness data evaluating ablation and surgical extirpation is plagued by profound selection bias and short-term follow-up. Well-controlled prospective studies with long follow-up must be done to better characterize the role of ablation in the therapeutic armamentarium for localized RCC.

As previously mentioned, the widespread application of cross-sectional imaging has resulted in more frequent diagnosis of small, localized renal masses of uncertain clinical significance. Much like prostate cancer, the changing epidemiology of RCC has generated significant interest in active surveillance for small renal masses. Furthermore, analysis of population data has revealed increased rate of treatment for renal cell carcinoma, however, the death rate from the disease has paradoxically increased [149]. These data suggest that commonly treated small incidental renal tumors may be of little clinical significance and may not require active treatment. Indeed, numerous series have documented the relatively slow growth of small renal masses. Haramis et al. reviewed the Columbia University experience of patients with small renal masses subject to long-term follow up and found the median growth rate to be 0.15 cm per year with only 4.5 % of patients requiring delayed intervention.

No patient in this series suffered from metastatic disease or cancer-related death. Other series have corroborated these data and have found that upwards of one-third of small renal masses demonstrate zero net growth at a median follow-up of 29 months [150]. Additionally, a meta-analysis determined that the risk of progression to metastatic disease was equivalent in patients undergoing active surveillance (AS) when compared to those undergoing extirpative surgery or ablative therapy [148]. Furthermore, retrospective data indicate that delayed intervention secondary to increase in tumor size does not portend any prognostic implication [151]. Taken together, these data suggest that AS is a reasonable treatment strategy for patients with small renal masses who are too debilitated to undergo active intervention or who are unwilling to accept the potential risks of such interventions.

Treatment of Metastatic Disease in the Elderly

One of the most salient questions in the management of elderly patients who present with metastatic disease is whether this group stands to benefit from cytoreductive nephrectomy. Overall survival for elderly patients who undergo cytoreductive nephrectomy in the setting of metastatic RCC has been shown to be similar to that of younger patients, albeit in a small sample size. However, cytoreductive nephrectomy is associated with an increased risk of perioperative mortality in those ≥75 years of age. Specifically, Kader et al. found the risk of perioperative mortality to be 21 % in those older than 75 years and 1.1 % in younger patients. The risk of a major operation in the setting of metastatic disease must be balanced with that of potential benefit on an individual basis in this age group [152].

Over the past decade numerous targeted systemic therapies have been approved for the treatment of metastatic RCC. While these therapies are not curative in the setting of advanced disease, treatment can provide improvement in progression free survival; most commonly in patients with lower tumor burden and good performance status [153]. While there are few trials that specifically address comparative effectiveness of targeted therapy in the elderly, the available data does suggest that treatment efficacy is similar in older and younger populations. Subgroup analysis of the TARGET Study, a randomized trial evaluating the efficacy of sorafenib compared to placebo in patients who had been previously treated with systemic therapy, demonstrated similar median progression-free survival amongst sorafenib-treated patients older and younger than 70 years. The risk of adverse events was similar amongst age groups, however, there was a slightly higher risk of grade 3 and 4 adverse events in the elderly (45.7 % versus 36.7 %, respectively) [154]. Furthermore, in an Advanced Renal Cell Carcinoma Sorafeib (ARCCS) expanded access program in which sorafenib was made available to patients not eligible for a clinical trial, there was no observed difference in either response rates or adverse events between younger and older patients [155]. Phase III randomized data comparing sunitinib and interferon-alpha revealed no difference in clinical benefit and objective response rates between older and younger patients. Additionally, no differences in adverse events were identified between cohorts [156]. These data indicate that

commonly used systemic therapies for metastatic renal cell carcinoma are safe and effective in the elderly. Longer follow-up and further investigation will be required to identify the optimal treatment paradigm for advanced disease in the elderly.

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Chapter 8
Use of Adjunctive Services

Mary Ann Forciea

Introduction

Older patients present for care with a wide range of functional abilities, reside in a spectrum of locations, and require a variety of supportive services for care after active treatment. This chapter is designed to help you

- Understand the functional requirements for transfer or discharge to different sites of senior living
- Understand the support services available to older patients wherever their discharge location
- Improve your ability to gather historical or medical information about older patients
- Improve your communication with outside caregivers to improve after-care

Sites of Care *(See Table 8.1)*

The commonly encountered residential locations of older patients will be reviewed in this section, with attention to functional status requirements for that site, medical/nursing support available, medicare coverage considerations, and monthly costs.

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Table 8.1 Characteristics of sites of care

	Home	Assisted living/personal care home	Rehabilitation facility	Nursing home-short stay	Nursing home—longterm stay
Functional status	Independent[a]	Independent in ADLs, assistance with IADLs[a]	May be dependent in some ADLs, IADLS	Dependent in ADLs, IADLs	Dependent in ADLs, IADLs
Nursing staff	None (visiting nurse services available)	Most have limited daytime nursing staff coverage	Nurses, all shifts	Nurses, all shifts	Nurses, all shifts
Physician visits	Office visits Home care visits	Office visits Home care visits	Facility MDs available daily	Facility MDs/NPs see patient within 72 h of admission, then every 30 days. Urgent visits variably available. 24-h telephone coverage.	Facility MDs/NPs see patient within 72 h of admission, then every 30 days for 90 days, then every 60 days. Urgent visits variably available. 24-h telephone coverage
Medicare coverage	Office visits, home care visits, short-term skilled VN agency services	Office visits, home care, short-term, skilled VN agency services	Covered	First 21 days covered, then decreasing coverage	Not covered May transition to Medicaid coverage
Average monthly cost 2011		$4,000–6,000			$10,000–12,000 for private payment

ADLs Activities of Daily Living (bathing, toilet use, dressing, eating, mobility), *IADLs* (shopping, travel, financial management, telephone, cooking, taking medications, laundry, housekeeping), *VN* visiting nurse, *MD* physician, *NP* nurse practitioner

[a]In many cases, can purchase additional services to remain at this level in spite of increasing deficits

Table 8.2 Functional status

Activities of daily living (ADLs)	Instrumental activities of daily living (IADLs)	
Bathing	Cooking	Laundry
Dressing	Shopping	Housekeeping
Toilet use	Travel	Telephone use
Eating	Managing finances	
Mobility	Managing medications	
Transfers from bed to chair		

Home Care

The vast majority of older patients reside in their own homes. These patients, either on their own or with the support of family, manage their own needs, and are independent in Activities of Daily Living (ADLs) and Instrumental Activities of Daily Living (IADLs)—see Table 8.2.

Patients should have primary care practitioners and make office visits; many areas of the country have house call practitioners who can visit homebound seniors to provide ongoing primary care [1]. The American Academy of Home Care Physicians has a website with access listings for house call providers (http://www.aahcp.org).

Older patients with temporary needs for nursing oversight following a hospitalization or outpatient procedure can be referred to a *visiting nurse agency*. These multi-service organizations provide short-term skilled nursing services (wound care, medication monitoring and adjustment, home assessment, and teaching), rehabilitation services from physical, occupational, and speech therapy, social work, and some specialty nursing services such as wound care and ostomy care. Some agencies have expanded to provide home intravenous support and nutrition support; these agencies are often hospital owned and managed. For residents who require ADL support, temporary home health aides can be provided for short periods. The costs of care are usually covered by Medicare, but may require pre-authorization in Medicare managed care. The duration of care extends as long as the skilled care needs can be documented: as long as progress towards goals of care is being made. Once the patient has stabilized or reached a plateau in status, services are withdrawn. Visiting Nurse Agency episodes of care rarely exceed 6 weeks.

For patients who require long-term supportive care services at home, some special programs have been developed. Patients and families may privately pay companions or home health aides to provide care. In many areas of the country, assistance is available to help support patients and families in need of services at home. These programs are supported mainly through Medicaid programs of the states and vary widely. The programs are coordinated by a network of *Area Agencies on Aging* which are located in every county and provide information and access to state and federal programs available in a region. Local agencies can be accessed through the website of the National Association of Area Agencies on Aging: http://www.n4a.org.

An interesting innovation in the care of the frail elderly has been the development of *Programs of All-Inclusive Care of the Elderly* (*PACE*) programs throughout the nation [2]. These programs offer to Medicare/Medicaid eligible seniors a coordinated menu of medical and social programs at specialized sites. Because PACE sites are equivalent to managed care and are capitated for each member, sites often develop specialized referral networks for their patients.

Seniors who find the maintenance of their homes too difficult can opt for *senior housing* in specialized buildings which also offer increased security. Rent may be income-linked; many of these buildings are built with federal support for low-income elderly. Larger facilities may offer some social work access, but no health or social services are mandated in these buildings, and the residents are expected to be independent in their apartments.

Assisted Living Facilities/Personal Care Homes

The fastest growing segment of housing for older people is the *Assisted Living Facility* (*ALF*). These often "for-profit" buildings offer apartments of various sizes as well as dining rooms providing daily meals, and often some program of activities. Residents are expected to be independent within their apartment (ADL independent). Many offer housekeeping, laundry, and medication oversight as additional charges. Some facilities offer "memory" programs with additional activities and oversight—these specialized areas are usually more expensive. Residents or families are responsible for obtaining medical care which is usually provided in an outside physician's office. State regulation of these facilities ranges from nonexistent to nascent; services may vary widely from state to state, and even county to county. Costs are generally covered by patients and families themselves; some states are beginning to allow Medicaid payments to ALFs. While these facilities are generally attractive physically (resembling apartments rather than nursing homes), these sites generally cannot meet the life-long requirements for care for residents with progressive illnesses such as dementia. Residents will need either to relocate again to a nursing home when they become ADL dependent, or purchase increasingly expensive amounts of care in the ALF.

The concept of electronic monitoring/assistance of older patients living in their own homes is referred to as "*Ambient Assisted Living*", and attempts to expand care for patients living in their own homes. Devices can be focused on monitoring (thermal sensors, pill box sensors, fall detection), or on care assistance (pill reminder alerts, orientation systems). Some of these devices are being incorporated into Assisted Living Facilities to increase monitoring and care. Very few studies document the effectiveness of such devices in changing quality of life or safety.

Personal care homes also provide housing (usually in a shared bedroom) and meals for lower income patients. In most states, Medicaid will cover most of the costs of care for this level of service. Again, medical care is provided off site in a

physician's office; no nursing care is provided as a routine. Some homes will assist in medication oversight but many do not.

Rehabilitation Facilities

Older patients recovering from an acute illness or hospitalization can be referred to short stay *rehabilitation* facilities if they need physical, occupational, or speech therapy, and can tolerate at least 3 h of therapy daily. These facilities aim at preparing patients for discharge to their homes. Stays are covered by Medicare. Older acutecare patients may be declined by these facilities on referral because of patients' cardiopulmonary limitations on endurance, or on cognitive abilities to carry over each day's therapy to the next day. Cognitively intact older patients who were functionally independent on admission should not be routinely excluded from consideration for referral to rehabilitation facilities.

Long-term acute convalescent units (LTACs) have developed to serve inpatients with highly skilled but relatively stable needs such as long-term antibiotic therapy or ventilator-dependent patients recovering from acute illnesses. Stays are usually Medicare approved, but may require pre-authorization.

Nursing Facilities

Elderly patients who need short-term stays in *Nursing Facilities* for skilled care following illness or treatment may receive that care under Medicare. Nursing and rehabilitation services are provided as long as the patient is making progress toward defined skilled care goals. Medicare pays in full for up to 21 days of skilled care; Medicare pays a decreasing proportion of costs of care for longer stays if skilled care goal progress continues to be met. At the point that patients have returned to baseline or have stopped making progress, they must be discharged home or become long stay patients at a long-term nursing facility. In many facilities, this may involve a transfer from one area of the facility to another.

Long-term care in a nursing facility provides support for both ADL and IADLs. Nurses are available on all shifts, although at a reduced ratio from that seen in hospital settings. Physicians visit the facility based on the number of patients for whom they provide care. A medical director oversees care and sets protocols for care. Admitting orders are often telephoned to covering physicians; a newly admitted patient must be seen by his physician within 72 h of admission. Both because of the increasing acuity of patients admitted to long-term care, and to the sporadic nature of physician visits, some larger facilities are adding Nurse Practitioners to their staff [3]. Long-term care in nursing facilities is privately paid by patients/families, or by Medicaid programs. Quality comparisons for all Medicare certified facilities are

available at http://www.medicare.gov under "nursing home compare" A very small percentage of long-term care is covered by long-term care insurance.

Hospice

Hospice services are available to Medicare patients who wish to shift the focus of their care to quality of life, and who are felt to have less than 6 months of life remaining. The original focus of many hospice programs was on the end of life care of cancer patients; more modern programs have expanded to include all the major late life diagnoses such as dementia, heart failure, renal failure, and COPD. Because of their expertise in palliation of symptoms, many hospice programs have opened palliative care options which do not exclude active treatment during care. The focus on expected duration of care has also changed somewhat; patients are evaluated on admission and at regular intervals; patients who stabilize or improve on the hospice approach to care are transferred back to regular care with remaining hospice benefits placed on hold. The majority of hospice care in the United States is provided in patients' homes. Inpatient hospice units are becoming more available in the United States, and can offer respite to families or help with more difficult palliative needs. Hospice care provided to residents of nursing facilities is a new venue for hospice services with additional palliative care options for these residents and their families.

Continuing Care Retirement Communities

The past two decades have seen growth in the development of "communities" which provide housing for older people who are independent in their functional needs, but also include assisted living, and nursing facility level care for residents as they age in place. Both non-for-profit and profit models of such care exist. The models can be tightly controlled with a single administration managing medical care and transitions of care between levels, or may provide property management with individual accountability for health care. Since many of these communities require substantial entry fees, care in investigation of community management, finances, and social activities are necessary prior to entry.

General Considerations

Office-Based Care

Older patients seen in the office setting will most likely be living at home either independently or supported by family. Special considerations for these older patients are listed in Table 8.3. Telephone "menus" should always feature a "speak to office

Table 8.3 Office-based care of older patients

Allow time for information from a secondary source (in addition to the patient)
Spouse
Family
Outside records (nursing facility, assisted living facility)
Ask patients/family to repeat back important information
Test results
Treatment plans
Write down important information for patient/family to review after the visit
Refer patients to local visiting nurse agencies for temporary skilled care needs such as wound care, ostomy care teaching, or medication monitoring

staff" option mentioned early in the menu. Older office patients may have difficulty with access to the office, if long walks from parking or drop off areas are required. Due to the high incidence of multiple chronic conditions, more time may be required to satisfactorily complete the office visit. Patients and families who require temporary skilled nursing services such as wound care, ostomy care, or medication monitoring should be referred to local Visiting Nurse Agencies.

Patients who are residing in Nursing Facilities can be a special challenge in the office: they may arrive on stretchers or wheelchairs (requiring more space in the waiting area), have complex medical issues, and require facility forms for completion. These frail patients may be unable to tolerate long waiting times, or have pickup schedules arranged prior to the visit. Office staff should ask about plans for transportation. Information on diagnoses made, tests ordered, and treatment plans should always be sent back to the facility with the patient after the visit.

Hospital Care (See Table 8.4)

The hospital care of older patients can present many challenges which are discussed in many chapters of this book. This section will focus on information sharing between sites of care for hospitalized older patients.

While the advent and spread of electronic medical records (emr) has been of great benefit to older patients in ease and legibility of medical information, some cautions must be reviewed:

- Some patients may receive care from more than one health system; the emr may be incomplete.
- Medication lists may not correspond to actual medications, doses, or dosing intervals used by the patients. Medication reviews should always be checked with the patient/family on admission.
- Advance Directive status may change over time. Advance Directive status information should be confirmed during the admitting process.

Information gathering on older, newly admitted inpatients can be challenging. If the patients themselves cannot provide complete or reliable information, families or

Table 8.4 Tips for hospital care of older patients

In reviewing medications, ask patients which pills they actually take rather than relying solely on electronic lists
Alternate sources of admitting information for confused older patients:
Family members
Nursing facility transfer sheets
Nursing facility charge nurses
Primary care offices
Work with hospital discharge planning staff from time of admission on options for aftercare
Prepare discharge summary information prior to discharge to accompany patient to nursing facility or for transmission to the primary care office for follow-up care

Table 8.5 Tips for safe and effective discharge of patients to nursing facilities

Write medication or laboratory orders sufficient for 72 h
Send Rx for new medications, especially narcotics
Send discharge summary information to both the patient's primary care provider's office and to the admitting physician at the nursing facility

nursing facility staff can be telephoned. If information is needed from the patient's nursing facility, the charge nurse on the floor caring for the patient is often the best source of information.

Successful, efficient patient flow during the process of care requires team management from physicians, nurses, social workers, and discharge planners. The entire team should be aware of possible discharge needs for the patient from the time of admission, with updates as clinical situations change. Patients and families should be included in this planning process as early as possible.

The information regarding the hospital stay contained in the Discharge Summary should be shared with responsible providers as soon as possible on discharge. Ideally, summaries should accompany patients who are being discharged to other health facilities such as nursing homes or rehabilitation facilities. Summaries should be transmitted to Primary Care offices so that providers are prepared to participate in needed follow-up care. Critical, short-term treatment or assessment needs should be telephoned to these providers.

Optimal discharge arrangements for patients being transferred to long-term care (nursing or rehabilitation facilities) have some special requirements (See Table 8.5). Patients are being transferred from one team of providers (hospital) to another team (long-term care facility). All members of the team need to transfer information on diagnoses, test/procedure results, pending results, and plans for ongoing care. This information is shared in a variety of forms: state-mandated transfer forms (usually completed by nurses), discharge orders and summaries (usually completed by physicians, nurse practitioners, or physicians' assistants), social work, and rehabilitation assessments. Urgent or critical information should be shared by telephone contact at the time of transfer.

In most states, upon arrival in a nursing home following a hospital discharge, the patient will receive a thorough nursing assessment. Admitting orders, written by the discharging hospital physician, will be telephoned to the new nursing home physician for approval, that new physician will see the patient within 72 h of admission to the facility. Following that initial visit, nursing facility-based practitioners will see the patient monthly for the first 3 months, then every 2 months thereafter. Urgent visits for changes in medical condition are made at any time as needed.

Conclusions

Effective care of older patients requires an understanding of the network of support services and locations of care which may be required during recovery. Assessment of function is critical to appropriate planning for treatment and recovery. Options for increased care for patients in their homes in the community are usually coordinated through local Visiting Nurse Agencies. Short-term rehabilitation stays can be accomplished in rehabilitation facilities or in nursing facilities. Long-term care can be provided at home or in nursing facilities. For older, frail patients in home the burdens of treatment have begun to outweigh possible benefits, options for palliative hospice care at home or in an inpatient hospice should be offered to patients and their families.

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Chapter 9
Urology in the Nursing Home

George W. Drach and Edna Schwab

We, a urologist and a geriatrician, conduct patient Grand Rounds (some personal and some chart based) at our Philadelphia Veterans Administration Nursing Home on a monthly basis. Why? Because we find that this patient group, men and women confined to a long-term care (LTC) environment, harbor many urologic problems that require consultation and treatment. Several authors have recommended special attention to urology in the nursing home [1–3]. In particular, we agree with Pranikoff [1] that the major problems encountered in the nursing home are voiding dysfunction and incontinence and its consequences, indwelling catheters and their management, asymptomatic bacteriuria, symptomatic urinary tract infection (UTI), hematuria, and considerations of sexuality [4]. We add to that our frequent encounters with the problems of management of prostate cancer and stone disease in the chronically ill or bed-bound and often demented patient. Of course, with the decline in numbers of nursing home patients over the past years (Fig. 9.1), some of the urologic problems of the LTC patient will be transferred to the home-bound patient, but the problems continue to exist.

This chapter deals with each of these issues presented above. First we will discuss the problem of true prevalence of incontinence in the nursing home patient. According to Anger et al. [5], incontinence of newly admitted nursing home residents is greatly under-reported and is said to be in the range of 1–2 %. Their investigation of a National Nursing Home Survey revealed that over 50 % of females had

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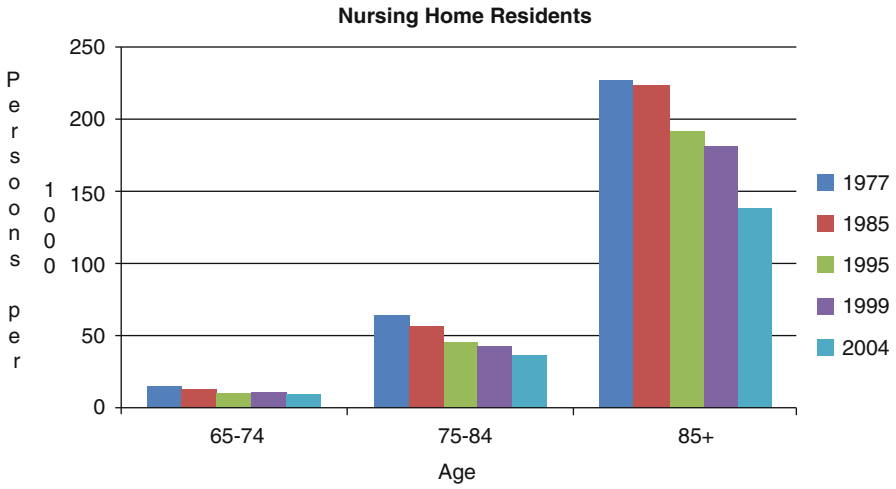

Fig. 9.1 Gradual decrease in the number of nursing home residents of all ages from 1977 to 2004 (Adapted from Centers for Disease Control and Prevention, National Center for Health Statistics [24])

"difficulty controlling urination" or needed assistance in using the toilet. Klausner and Vapnek [6] carried this observation further by evaluating female and male nursing home residents and pointed out that the incidence in females exceeds that in males by a ratio of 2:1. In a small study (83 patients) Rose and associates determined that patients with more incontinence measures by "pads per day" suffered also from worse nutritional status, more dementia and lower levels of mobility [7] Shih and colleagues [8] analyzed the labor costs associated with incontinence in nursing homes and estimated that individual added costs per patient per day were $13.57 or nearly $5000 annually. Incontinence therefore represents one of the greatest urologic problems in the nursing home. How is it dealt with?

Voiding Dysfunction and Catheters

Multiple problems may lead to incontinence in these patients: urethral sphincter weakness, UTI, urinary urgency or involuntary bladder contractions, bladder atony and/or overflow incontinence associated with obstruction. Hopefully the primary causes associated with the abnormal voiding function have been defined, but often "shotgun" methods (anti-muscarinic drugs or catheterization) begin without full evaluation. Foremost amongst these is use of bladder catheterization for the control of incontinence [9]. Newman et al point out that reduction in catheter use to treat incontinence is one of the mandates of the Centers for Medicare and Medicaid Services (CMS) issued in 2005. This, of course, helps in decreasing the related incidences of UTI, urethral erosion, urethritis and

epididymitis and especially in females, catheter expulsion. If the indwelling urethral catheter does become the method chosen, the next questions are: (1) how often should it be changed, especially if one is to reduce the risk of symptomatic urinary infection and (2) how should the catheter be cared for? These dilemmas present some of the strongest reasons for urologists to be well acquainted with nursing home care.

Priefer et al. [10] performed an interesting study of patients in a VA Nursing home. Catheters were changed in two random groups: group 1 only for acute infection or catheter obstruction (7 men), and group 2 on a regular monthly schedule as well as for infection or obstruction (10 men). Six of the former group (86 %) developed symptomatic UTI while only 3 of 10 in group 2 did so (30 %). Obviously, this was a limited study, but it seems to corroborate the usual advice to change indwelling urethral catheters on a monthly basis.

Nursing homes usually have available non-invasive devices for measurement of bladder residual urine volume. These assist the urologist in decisions about degree of obstruction or inadequate bladder emptying. If increased residual exists, then conservative treatment methods may lead to a satisfactory resolution, but again, an indwelling catheter is frequently attempted as the first intervention, rather than preferred alternate techniques such as sterile or clean intermittent catheterization (CIC) [11]. If the patient can perform CIC, then that is better for them. If it must be done by nursing personnel, the time requirements may seem excessive, but the proven decrease in symptomatic UTI for intermittent over indwelling catheterization pleads for the use of CIC [12]. Of course, if increased residual is related to outlet obstruction, some procedural intervention to relieve obstruction may be necessary. In the absence of obstruction, other simple procedures such as timed voiding, double voiding or expedited access to a commode may be the only interventions needed [3, 13].

When problems such as recurrent urethral erosion appear in a patient, the question of inserting a suprapubic tube arises. Our judgment often results from the success or failure of previous attempts to correct the voiding dysfunction: relief of outlet obstruction by surgical intervention in the up and about patient, intermittent catheterization in any patient where the obstruction or bladder atony cannot be overcome, use of condom catheters where incontinence exists without obstruction. When all these interventions that may be tried have failed, then perhaps a test of suprapubic catheterization may be performed with a percutaneous insertion under ultrasound guidance [14]. If this provides adequate improvement, a more permanent retention catheter can be placed by gradual size increases.

One of the complications that the suprapubic catheter helps to avoid is the meatal or urethral erosion sometimes associated with indwelling catheterization (Fig. 9.2). But another way to avoid the complication is to conduct educational programs for the staff charged with catheter management [16]. Proper draping of the drainage tube to avoid urethral tension, and attention to re-draping when the patient is repositioned resulted in a decreased number of these events in our experience.

Fig. 9.2 Severe urethral erosion associated with indwelling urinary catheter (From LeBlanc and Christensen [15])

Asymptomatic Bacteriuria and Urinary Tract Infection

Another of the significant problems encountered in the nursing home patient is the presence of bacteria in the urine: asymptomatic or symptomatic? We know that this is common in conjunction with long term indwelling catheter, but it also occurs in the catheter free patient. What is the significance of these bacteria? Juthani-Mehta [16] published an extensive review on this subject and presented precise requirements for diagnosis of asymptomatic bacteriuria versus UTI. One question that always arises is the validity of using a dipstick to detect infection. Perhaps the most important component here is that a negative dipstick strongly mitigates against bacteriuria and thus against UTI. However, any dipstick positivity must be followed by a properly collected urine specimen for culture.

Notably, the incidence of asymptomatic bacteriuria increases with increasing age and thus (from our Fig. 9.1) in community or nursing home populations, being barely 1–2 % until age 65, but over 6 % thereafter in community dwelling elderly. For those patients in LTC institutions, the prevalence is greater than 15 %. Sometimes this finding of bacteriuria is associated with symptoms of true infection: fever, painful urination and so forth. But these symptoms may not clearly

Table 9.1 Help in diagnosing UTI in nursing home patients (presence of at least three of four criteria) [15]

1. Fever greater than 100.4 °F
2. New or increased burning on urination, frequency or urgency
3. New flank or suprapubic pain or tenderness
4. Change in character of urine and/or worsening of mental or functional status

diagnose true UTI: "To date no constellation of symptoms is identified in older adults who have bacteriuria that can distinguish symptomatic from asymptomatic patients reliably in all situations" [16]. However, in the presence of symptomatic bacteriuria, presence of at least three of four criteria may be useful in deciding to treat (Table 9.1).

Hematuria

Another vexing problem seen in the LTC patient is hematuria. This may be found microscopically on routine urinalysis (and remember that to be considered significant by American Urological Assn criteria must be greater that 3 RBC/HPF in at one microscopic adequately collected urinary specimens) [17] or perhaps grossly present and noted by the patient or nursing personnel. Dipstick positivity for hematuria is not adequate for defining true hematuria. In any case, this drives the urologist toward standard evaluation including collection of specimen for cytology, anatomic imaging and cystoscopic examination. However, questions always arise about the necessity of such procedures in the bed-ridden demented patient or one with multiple co-morbidities for whom no significant intervention would be considered. In such situations, one must consult with responsible family or guardian or other individual with health care power of attorney.

Sexuality

One of the most poignant presentations of this subject occurs in the fictional book by F. Scott Peck, MD entitled "A Bed by the Window" [4]. This is the story of a LTC patient assigned to the inside bed of a double bedded room. Her greatest desire is to ultimately move to the window bed so that she can see the outside view every day. But throughout this book one is shown the various day-to-day activities within the LTC facility – and that includes sexual innuendo and encounters amongst patients and staff. Pranikoff has stated that "Sexuality in nursing home residents is neglected and often suppressed by staff", yet he continues by saying "surveys confirm that sexual interest and the need to show affection to another person remains important for nursing home residents". Certainly problems can occur when one patient pursues another, who may be partly or fully demented, or if a member of the staff

pursues a patient. He [1] encourages nursing homes to educate staff and to establish reasonable rules to allow appropriate relationships.

Urinary Stone Disease

Use of long-term indwelling urethral catheters leads to urinary infections as noted above [18]. Even the presence of a suprapubic catheter increases the risk of formation of bladder stone [14]. These infections result in increased incidence of cystitis and pyelonephritis [19], with the result that infection related stones occur. In addition, those patients with a genetic predisposition toward metabolic urinary stone disease continue to develop stones if in the LTC facility. Management of LTC patients with stone disease is complicated by lack of nearby imaging facilities or poor control of pain. If the stone is "quiet", it may be detected only because of the investigation stimulated by discovery of hematuria (see above). Fortunately, the advent of minimally invasive techniques for stone removal decrease significantly the risk to the chronically ill patient, but even at a minimum, any such procedure requires transfer to a fully equipped hospital.

Prostatic and Other Genito-urinary Cancers

Since the incidence of prostate cancer continues to increase with age and with the increased number of elderly men, it is inevitable that more LTC male patients will have prostate cancer. Techniques such as radical prostatectomy may or may not be indicated for the LTC patient, but more conservative methods such as radioactive seed insertion or external beam radiation may provide adequate therapy if the patient or responsible surrogate express desire for treatment. Of course, the concept of "watchful waiting" may always be instituted, especially for those with limited life spans or with many co-morbidities [20]. Sometimes the patient or surrogate may urge surgical intervention of some type against the urologist's advice. This event occurred in our experience when a demented, bed-ridden man of 84 years somehow had a PSA performed, and the result was greatly elevated. On examination the prostate was irregular and hard. Most of us would consider this presumptive evidence of prostate cancer. When these findings were discussed with his wife, she insisted that we perform a biopsy to "prove that he had cancer". We explained the multiple and potentially serious complications that might occur – but the insistence remained. We also pointed out the medical concept that it was not usual to obtain a biopsy if the result – a cancer – was not likely to be treated, as we believed to be the case for this patient. She indicated that if a cancer was found, she wished it to be treated. Prostate cancer of high grade was found, and in agreement with the patient's wife,

he was placed on anti-androgen therapy. This clinical story illustrates the difficulty one might have in dealing not only with the patient, but with the patient's surrogate. Yet in counseling this patient's surrogate, it was clear that diagnosis and treatment were strongly desired, in spite of our advice to the contrary [21].

Other urologic cancers such as bladder and kidney increase greatly with increasing age so that one must remain alert to these possibilities. Once again, the signal often is hematuria, followed by the complete evaluation. Minimally invasive methods such as partial nephrectomy, or robotic cystectomy and diversion that would not have been possible in the frail elderly LTC patient may now be successfully completed when the operative plan includes all the precautions necessary for the elderly and partly or wholly disabled patient.

Ethics and the Functionally and Cognitively Impaired Patient

The decision to pursue any medical evaluation and treatment for an impaired long term care resident is very individualized and should be determined by several factors. These include the potential risks versus benefits of specific diagnostic evaluation and treatment, the surrogate decision maker's wishes or directives of a patient's living will. The purposes are to maintain the patient's present functional and cognitive status as well as their quality of life. For instance, one would likely not pursue an intensive and invasive evaluation of hematuria in a long term care resident who is moderately to severely demented, lacks functional capacity, and requires complete nursing assistance for all activities of daily living. After discussion of the problem by the medical team and surrogate, a reasonable approach to hematuria in such a patient would be to obtain a urinalysis checking for evidence of infection and cytology for abnormal cells. If infection or abnormal cells were not present, pursuing an evaluation of the prostate, bladder and upper tracts would likely not yield information that would improve the survival and quality of life of this resident. Palliative approaches to any symptoms the resident may express would be provided including pain control with analgesics, bladder irrigation if blood clots obstruct urinary flow or relief of obstruction with an indwelling Foley catheter [22].

Some long term care residents will have an advance health care directive such as a living will which provides a written statement of their desires regarding life sustaining treatment and other medical care when he/she becomes incompetent. When these document(s) are not available then the health care team will need to discuss risks, benefits, and treatment options with the health care agent or health care power of attorney. If neither is available, then the health care team must provide the best quality of life care available. When possible, good communication between health care providers and any health care agents will lead to a thoughtful and palliative approach to the care of the long term care resident with end stage disease [23].

Conclusion

Patients in nursing homes, or LTCs, harbor a myriad of urologic problems. Urologists often do not become involved with nursing homes because of distance, difficulty dealing with aged elderly patients, or in dealing with the complex Federal and Medicare related regulations. But, as shown throughout this Chapter, patients in nursing homes may have many urologic problems, most of which can be improved by simple and conservative urologic interventions. Communication between the urologist and the nursing home nurses and physicians, and occasional onsite consultations [3], lead to improved urologic care of the patients and therefore their enhanced comfort and quality of life.

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Chapter 10
Lower Urinary Tract Symptoms

Amy M. Pearlman, Ariana L. Smith, and Alan J. Wein

Introduction

The lower urinary tract consists of interrelated structures including the bladder, urethra, smooth, and striated sphincters, pelvic floor muscles, and the prostate gland in men with a common function of providing effective urinary storage and voluntary urinary expulsion. These functions are achieved in two discrete phases of micturition [1].

Phase one involves filling and storage of urine in the bladder and is accomplished through:

1. Accommodation of increasing volumes of urine at low intravesical pressure
2. Appropriate sensation of bladder filling without allodynia
3. A bladder outlet that is closed at rest remains closed despite increases in intraabdominal pressure
4. The absence of involuntary detrusor contractions (IVCs)

Phase two involves voiding and complete emptying of the bladder and is accomplished through:

1. Coordinated contraction of the bladder smooth muscle of adequate magnitude and duration

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2. Concomitant lowering of resistance at the level of the smooth and striated urethral sphincter
3. The absence of anatomic obstruction

During normal physiologic filling, bladder sensation is nearly imperceptible and inhibitory reflexes prevent bladder contraction while the guarding reflex increases striated sphincter activity. At or near capacity, the sensation of bladder fullness is responsible for initiating voluntary emptying of the bladder. Coordinated contraction of the bladder smooth muscle and relaxation of the urethral smooth and striated muscle leads to decreased outlet resistance, funneling of the bladder outlet, and facilitates complete bladder emptying. In the healthy adult, the facilitory and inhibitory neurologic impulses that regulate these processes are under full conscious control [2].

Lower urinary tract dysfunction is a term that has replaced voiding dysfunction as a descriptor of a broad category of abnormalities resulting from disruption of any one of the factors listed above; essentially a failure to store, a failure to empty, or any combination of these factors. Lower urinary tract dysfunction can result in what has been termed *lower urinary tract symptoms*, or LUTS [3]. The term "prostatism," previously used to refer to male urinary tract symptoms of any cause, has been abandoned due to confusion over the causal relationship between these symptoms and the prostate.

Several age-related changes in lower urinary tract function can develop, producing, at times, bothersome LUTS. Prostatic growth increases with age in men and may lead to benign prostatic enlargement (BPE) with patients complaining of hesitancy, decreased force of urinary stream, incomplete bladder emptying, and even frank urinary retention. The diagnosis of overactive bladder (OAB) increases with age in both men and women and consists of symptoms such as urgency, urinary frequency, nocturia, and urgency urinary incontinence (UUI) [4]. Other types of urinary incontinence are also common in the geriatric population; these include stress urinary incontinence (SUI), over flow incontinence, and mixed urinary incontinence.

A variety of symptoms and classification schemes for these symptoms exists. The most popular divides LUTS into filling/storage symptoms and voiding/emptying symptoms. For purposes of this chapter, however, symptoms will be classified into three broad categories: (1) LUTS suggestive of obstruction, (2) LUTS suggestive of OAB, and (3) Urinary Incontinence (Table 10.1). Many patients, however, present with a combination of symptoms coming from more than one of these categories [5].

LUTS Suggestive of Obstruction

LUTS suggestive of obstruction occur during the voiding/emptying phase of micturition or immediately following. Patients may experience one or a multitude of urinary symptoms of varying severities. Patients tend to seek care when symptoms become bothersome, interrupt sleep, or lead to embarrassment.

Table 10.1 Lower urinary tract symptoms

Obstructive symptoms	Overactive symptoms	Incontinence symptoms
Hesitancy	Frequency	Urinary incontinence
Decreased force of stream	Nocturia	Stress incontinence
Intermittency	Urgency	Urgency incontinence
Straining	Urgency incontinence	Mixed incontinence
Position-dependent micturition	Increased sensation	Postural incontinence
Incomplete emptying	Dysuria	Nocturnal enuresis
Double voiding	Bladder pain	Continuous incontinence
Post void dribbling		Insensible incontinence
Urinary retention		Coital incontinence

Symptoms suggestive of obstruction are described below [6].

Urinary *hesitancy* is the complaint of a delay in initiating the urinary stream.

Decreased *force of urinary stream* or poor flow is the complaint of a slower stream than previously appreciated or a slower stream than their peers.

Intermittency is the complaint of urinary flow that stops and starts one or more times during the voiding phase.

Straining to void is the complaint of needing to exert effort by Valsalva, suprapubic pressure, or other means of increasing abdominal pressure in order to initiate or maintain the urinary stream.

Position-dependent micturition is the complaint of having to contort one's body into a specific position in order to improve the force of urinary stream or bladder emptying.

Incomplete bladder emptying is the complaint that the bladder is not empty immediately after voiding.

Double voiding or the need to immediately re-void is the complaint that further micturition is needed soon after voiding.

Post void dribbling is the complaint of involuntary urinary leakage immediately after voiding.

Urinary retention is the complaint of the persistent inability to pass urine.

Etiology of Obstructive Symptoms

The etiology of obstructive symptoms may be anatomic, secondary to an enlarged prostate gland in men, bladder neck obstruction, urethral stricture, urethral compression/fibrosis in women, or pelvic organ prolapse in women. The etiology of symptoms may also be functional, secondary to detrusor striated or smooth sphincter dyssynergia, a fixed bladder outlet, Fowler's syndrome in women, or poor bladder function (impaired bladder contractility). On occasion, LUTS suggestive of obstruction may exist in the absence of any anatomic or functional cause.

Increased outlet resistance is a much more common phenomenon in men than in women, with BPE being the leading cause. Benign prostatic hyperplasia (BPH)

refers to typical histopathologic findings of glandular and stromal proliferation that occur in nearly all men if they live long enough. The location of this growth within the prostate gland, surrounding and adjacent to the prostatic urethra (in the transitional and central zones), is what leads to voiding symptoms (Fig. 10.1). In many men however, the presence of BPH is confirmed pathologically in the absence of voiding symptoms. BPE refers to the increased size of the prostate but implies that a benign pathology has been confirmed. Benign prostatic obstruction (BPO) is a form of bladder outlet obstruction and this term is used when the cause of anatomic obstruction is known to be due to BPH. When histologic confirmation has not been made, preferred terminology is "LUTS suggestive of BPO" [7].

The prevalence of BPH on autopsy increases with age with 25 % of men 40–50 years, 50 % of men 50–60 years, 65 % of men 60–70 years, 80 % of men 70–80 years, and 90 % of men 80–90 years showing histopathologic change [8]. Similarly, the prevalence of bothersome LUTS as measured by validated questionnaire, the American Urologic Association Symptom Score (AUASS), increases with advancing age [9]. However, clinical BPH varies widely with only a small percentage of those with histologic findings presenting for treatment of bothersome LUTS. Importantly, the size of the prostate gland is not linearly correlated to urodynamic evidence of obstruction or to severity of symptoms and therefore cannot be used as an indicator for treatment [10]. Similarly, small changes in prostatic size and tone can greatly improve LUTS, thus explaining the large beneficial effects seen from medical management.

A basic evaluation of men presenting with LUTS should include a thorough medical history, including the nature and duration of LUTS. Additional history should include any genital or sexual symptoms, prior urinary tract manipulation or surgery, and medication assessment. Physical exam should include a digital rectal exam to assess prostate size, consistency, presence of nodules, and anal sphincter tone. Palpation of the bladder to rule out distension should be performed and a basic neurologic assessment of motor and sensory function in the perineum and lower extremities is warranted. Urinalysis in the form of a dipstick should be carried out, with further evaluation if abnormalities are seen. In the evaluation of patients with LUTS suspected to be due to BPH there is no consensus on routine prostate-specific antigen (PSA) testing. Despite a lack of correlation between prostate symptoms, histology, size and even flow rate, an important relationship with PSA does exist. PSA, in men with BPH and no evidence of cancer, correlates with total prostate volume and is a predictor of the risk of acute urinary retention and ultimate need for surgery. Furthermore, it can be useful as a parameter for prognostic value for BPH progression and response to treatment [11–14]. Essentially, men with larger prostate glands and higher PSA values are at greater risk of experiencing further prostatic growth, worsening LUTS, progression to acute urinary retention and surgical intervention for their condition. Inevitably however, the routine use of PSA in this population will lead to several unnecessary prostate needle biopsies with their resultant complications, and diagnosis of clinically relevant and clinically irrelevant prostate cancer. The risks and benefits of PSA testing should be discussed with the patient.

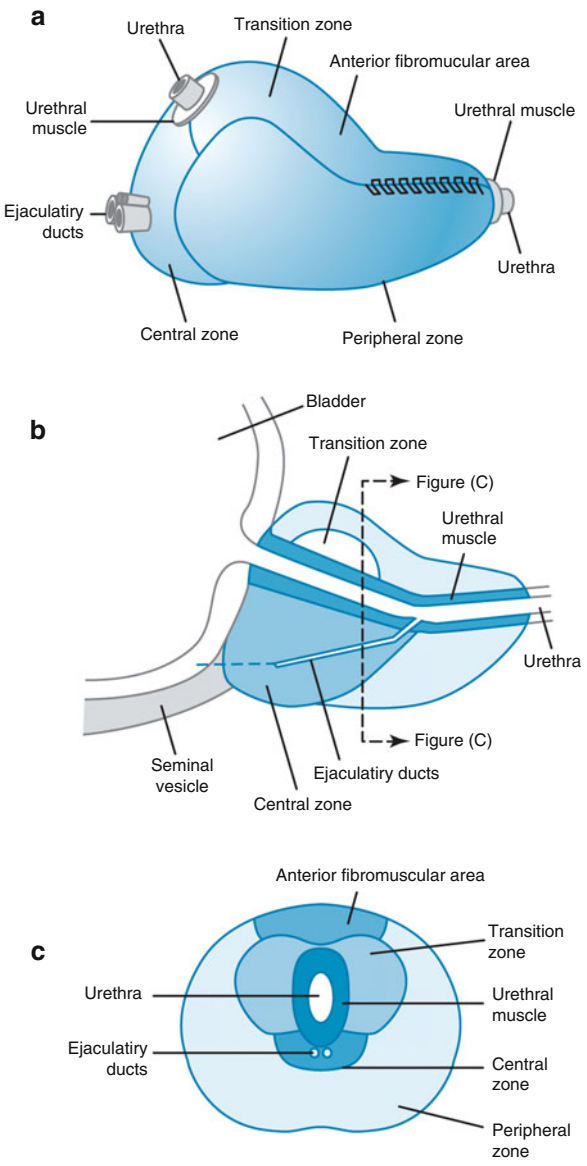

Fig. 10.1 Prostatic zonal anatomy (**a**) schematic, (**b**) sagittal cross-section, (**c**) transverse cross-section (Adapted from Hanno et al. [78])

A quantitative assessment of LUTS and degree of bother is recommended at the time of initial evaluation. The AUASS is a noninvasive, valid, reliable, and responsive index that correlates to the magnitude of urinary problems attributed to BPH (Table 10.2). A score of 7 points or less is considered mild LUTS, 8–19 points moderate LUTS, and 20–35 points severe LUTS. An additional quality of life measure allows for assessment of bother on a scale of 0–6 (delighted to terrible). This tool allows monitoring of symptoms over time, either in response to treatment or in

Table 10.2 American Urologic Association symptom index for benign prostatic hyperplasia (range from 0 to 35 points)

	Not at all	Less than 1 time in 5	Less than half the time	About half the time	More than half the time	Almost always	
1. Over the last month how often have you had a sensation of not emptying your bladder completely after you finished urinating?	0	1	2	3	4	5	
2. Over the last month how often have you had to urinate again less than 2 h after you finished urinating?	0	1	2	3	4	5	
3. Over the last month how often have you found you stopped and started again several times while urinating?	0	1	2	3	4	5	
4. Over the last month how often have you found it difficult to postpone urinating?	0	1	2	3	4	5	
5. Over the last month how often have you had a weak stream while urinating?	0	1	2	3	4	5	
6. Over the last month how often have you had to push or strain to begin urinating?	0	1	2	3	4	5	
7. Over the last month how many times did you most typically get up to urinate from the time you went to bed until the time you got up in the morning?	0, none	1 time	2 times	3 times	4 times	5 or more times	
AUA symptom index score: 0–7 mild, 8–18 moderate, 19–35 severe symptoms						Total	

Quality of life due to urinary symptoms							
	Delighted	Pleased	Mostly satisfied	Mixed about equally satisfied and dissatisfied	Mostly dissatisfied	Unhappy	Terrible
1. If you were to spend the rest of your life with your urinary condition just the way it is now, how would you feel about that?	0	1	2	3	4	5	6
Quality of life assessment index (QOL) =							
Quality of life assessment recommended by the World Health Organization							

Adapted from Wein and Lee [7]

the absence of treatment. The AUASS cannot be used as a diagnostic test or screening tool for BPH as it is nonspecific for BPH. In fact, women with OAB often have very high scores. Neither PSA nor AUASS can replace a thorough history and physical exam in the evaluation of LUTS felt to be secondary to BPH.

A voiding diary should be completed by the patient to document the number of daily voids, the distribution of voids during the day and night, the volume voided, and fluid intake. Other parameters, when present, such as urgency and leakage of urine, should also be documented.

The natural history of BPH is such that slow progression of symptoms over time is expected. Approximately 50 % of the time, patients with significant outlet obstruction develop overactive symptoms producing a combination of symptoms that exist during bladder filling and emptying. There has been a recent interest in initiating treatment to stabilize symptoms, reverse the natural progression of BPH, and avoid undesirable effects. Most men who seek treatment ultimately do so because of the bothersome nature of their symptoms which affects their quality of life. Treatment involves relief of the obstruction either by anatomic removal of the prostatic bulk or pharmacologic reduction in prostatic tone (alpha blockers) or size (5-alpha reductase inhibitors). Generally, relief of obstruction results in diminution of OAB symptoms; although, these symptoms may return as the patient ages.

Primary bladder neck obstruction (*PBNO*) is a condition where the bladder neck fails to open adequately during voiding resulting in poor urinary flow [15, 16]. It is found most commonly in young to middle aged men, but may be seen in women and children, as well [17, 18]. Symptoms are similar to those seen from prostatic obstruction, but on examination, an enlarged prostate is not appreciated. In many situations, patients go undiagnosed for many years and undergo multiple empiric treatments with various medications including antibiotics. The diagnosis is made urodynamically with confirmation of high pressure low flow voiding and fluoroscopic imaging confirming a failure of the bladder neck to relax with voiding (Fig. 10.2). Initial treatment includes a trial of alpha blockers; however, often definitive relief with transurethral incision of bladder neck (TUIBIN) is needed.

Bladder neck contracture (*BNC*) is generally iatrogenic, occurring after radical prostatectomy, outlet reduction for BPO, transurethral resection of the prostate, or various other alternative strategies for treating BPO. The contracture is composed of scar tissue, preventing appropriate funneling of the bladder neck during voiding. The scar tissue may progress to complete luminal obliteration preventing any flow or urine or passage of instruments through the urethra. BNC rarely responds to medication therapy and commonly requires dilation or more definitive transurethral incision or resection of the bladder neck. Urethral stents have been used with mixed outcomes in attempts to avoid anastamotic urethroplasty, a technically challenging operation. The major risk of these interventions is urinary incontinence often requiring subsequent artificial urinary sphincter placement. This, however, should be delayed until confirmation of sustained opening of the contracture is confirmed. Recalcitrant contractures require major reconstructive surgery such as appendicovesicostomy, augmentation cystoplasty, or continent catheterizable stomas [19]. Chronic suprapubic tube drainage has been used as a less invasive means of management.

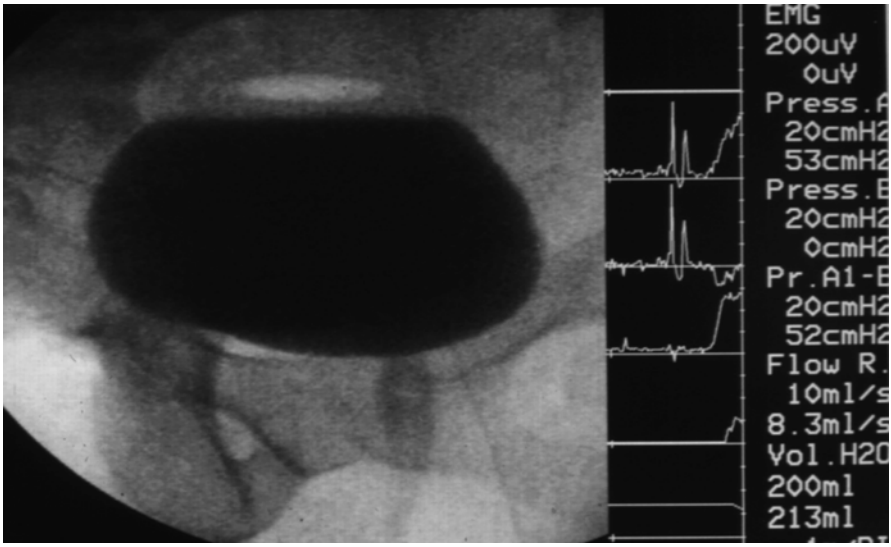

Fig. 10.2 Primary bladder neck obstruction documented fluoroscopically with failure of the bladder neck to funnel during voiding. A high pressure (52 cm H_2O) low flow (8.3 mL/s) pattern was seen on the urodynamic tracing

Urethral strictures can occur in men and women but are more common in men. They can result from urethral infections such as chlamydia or gonorrhea or may result from prior urethral instrumentation or trauma [20]. Scar tissue narrows the urethral lumen and can vary in length from under a centimeter in length to several centimeters [21]. Progressive obstructive symptoms tend to develop with narrowing of the urinary stream, incomplete bladder emptying, and eventual acute urinary retention in some patients. Complications including urinary tract infection, prostatitis, epididymo-orchitis, bladder diverticuli, bladder stones, bladder wall thickening, and eventual bladder decompensation and hydroureteronephrosis can occur [22]. Left untreated, periurethral abscess formation with subsequent urethrocutaneous fistula formation to the perineum may also occur. Urinary flow rate studies in patients with strictures generally show a low flow rate with a plateau pattern indicative of a slow protracted urine flow. Flow rates can also be helpful in detecting recurrent stricture in patients who have undergone previous successful treatment. Post void residual urine volumes are usually done concomitantly and, together with flow rate, provide a measure of voiding efficiency. Definitive diagnosis of a urethral stricture is made with either a retrograde urethrogram (RUG) and voiding cystourethrogram (VCUG) or cystoscopy. A RUG/VCUG can show the length as well as the caliber of the stricture. These studies are an important step in surgical planning for reconstruction of the urethra. Initial treatment generally involves dilation or incision of the stricture endoscopically with a direct visual internal urethrotomy (DVIU). But, less than half of patients will be cured with these interventions [21]. For patients who elect a more definitive primary therapy, urethroplasty can be a highly effective and cost effective option. Urethroplasty can be performed in an end to end fashion or

augmented with buccal mucosa, penile skin or other flaps or grafts. Self catheterization or calibration can be an effective means of preventing recurrence and preventing future surgical intervention [23, 24]. Patient compliance, however, tends to limit the utility of this option. Urethral stents have won the favor of a few urologists with most others finding poor results, recurrent strictures, and great difficulty removing them should they wish to [25]. In patients who have failed multiple interventions including urethroplasty, perineal urethrostomy is a viable option that prevents the need for further surgery.

In women, bladder outlet obstruction may be the result of urethral compression from external vaginal cysts, urethral diverticuli, urethral strictures, or cancerous growths. It may also occur secondary to fibrosis of the urethra which prevents appropriate dilation and funneling during voiding and usually results from urethrovaginal atrophy. Pelvic organ prolapse can also produce anatomic obstruction due to kinking of the urethrovesical junction. Most commonly today, obstruction in the female is iatrogenic, secondary to treatment of urinary incontinence with various anti-incontinence procedures such as slings, retropubic suspensions, and urethral bulking agents. Vague symptoms may be present in women, often delaying diagnosis and confusing treatment. Urodynamics can be helpful, but no definitive pressure flow criteria exist to firmly diagnose obstruction in women. Alleviation of obstruction generally produces a marked improvement in voiding symptoms, but a high index of suspicion for obstruction must be present for proper diagnosis, especially in women who have undergone prior pelvic floor reconstruction. Urinary retention in young women in the absence of neurologic disease may be the result of *Fowler's syndrome*. Generally the condition comes on with symptoms of lower abdominal discomfort, inability to void for a day or more, and little urinary urgency or bladder sensation. Often these patients have concomitant polycystic ovarian syndrome. Patients are generally found to have over one liter of urine in their bladders and urodynamics show acontractility. A unique EMG abnormality is present that impairs sphincteric relaxation. The only successful treatment is neuromodulation; however, this is not effective in all patients [26].

Detrusor striated or smooth sphincter dyssynergia refer to phenomena in which the sphincteric mechanisms fail to normally relax (open) concomitant with bladder contraction, thereby preventing normal micturition and producing a functional obstruction to the flow of urine. Straited sphincter dyssynergia occurs almost exclusively in patients with suprasacral neurologic disease. During urodynamic studies, an increase in pelvic floor EMG activity, rather than a decrease, in the presence of an obstructive voiding pattern is suggestive of this condition [27]. A non-neurogenic condition with similar findings, termed Hinman's syndrome, is felt to be the result of involuntary contraction of the sphincteric mechanism during voiding. This is thought to be a learned behavior that can be unlearned with appropriate pelvic floor and biofeedback training. Smooth sphincter dysfunction, also referred to as bladder neck dysfunction, is seen almost exclusively in men and is generally not associated with neurologic disease, the notable exception being in both sexes with autonomic dysreflexia.

Fixed bladder outlet or resting residual sphincter tone is another neurologic phenomenon where the urethral smooth sphincter is competent, but non-relaxing and the striated sphincter is fixed thereby preventing funneling and opening of the urethra during voiding. Generally patients have mixed symptoms with incontinence

and incomplete bladder emptying and their striated sphincter is not under voluntary control. Voiding generally occurs by Credé's maneuver [27]. A typical example is the myelodysplastic patient with neurogenic LUTS.

Bladder underactivity or poor bladder contractility may result from alterations in neuromuscular mechanisms necessary for initiating and maintaining a normal bladder (detrusor) contraction. Inhibition of the voiding reflex in a neurologically normal individual may also occur; it may be psychogenic or secondary to increased afferent input from the pelvic and perineal areas. Non-neurogenic causes also include impairment of bladder smooth muscle function which can result from over distension, drugs, severe infection, or fibrosis [28].

LUTS Suggestive of OAB

LUTS suggestive of OAB, previously referred to as irritative LUTS and now commonly referred to as OAB, occur during the filling/storage phase of micturition. Overactive symptoms increase with age in both men and women and consist of symptoms such as urgency, frequency of urination, nocturia, and urgency urinary incontinence (UUI).

OAB symptoms are described below [6].

Daytime urinary *frequency* is the complaint of more frequent micturition than previously considered normal.

Nocturia is the complaint of interruption of sleep one or more times due to the need to void.

Urgency is the complaint of a sudden, compelling desire to void which is difficult to defer.

Urgency urinary incontinence is the complaint of involuntary loss of urine associated with urgency.

Increased bladder sensation is the complaint of the desire to void at an earlier time point or smaller bladder volume than previously experienced.

Dysuria is the complaint of burning or discomfort during voiding.

Bladder pain is the complaint of suprapubic or retropubic pain, pressure, or discomfort, related to the bladder and usually increasing with bladder filling. It may persist or be relieved with bladder emptying. This is generally not a part of the OAB symptom complex.

Etiology of OAB Symptoms

OAB syndrome is the combination of urinary urgency, usually accompanied by frequency and nocturia, with or without UUI, in the absence of urinary tract infection or other obvious pathology [6]. Overactivity of the bladder during the filling/storage phase of micturition may be the result of involuntary bladder contractions, impaired

detrusor compliance, or a combination of the two. Involuntary bladder contractions are commonly seen in the presence of neurologic disease, bladder outlet obstruction, SUI (presumably due to entry of urine into the proximal urethra eliciting a reflex bladder contraction), pelvic organ prolapse, bladder or ureteral calculi, urethral pathology, aging, increased afferent input secondary to inflammation or irritation, or may be truly idiopathic [28]. The involuntary muscle contraction may occur, in some individuals, due to the release of excitatory neurotransmitters, specifically acetylcholine (Ach), from the urothelium during filling/storage [29]. Ach activates afferent nerve receptors leading to a premature or heightened sensation of distention or bladder fullness, urgency, or pain. In the setting of urgency incontinence, it is generally believed that an involuntary contraction occurred precipitating the leakage. Urodynamics can confirm the presence of involuntary contractions, termed detrusor overactivity (DO); however, this imperfect test may show DO in the absence of clinically relevant symptoms and may fail to show DO when a very high index of suspicion exists. Furthermore, repeat studies are often inconsistent [30]. Several possible pathophysiologic mechanisms for OAB have been described including (1) reduced suprapontine inhibition, (2) damaged axonal paths in the spinal cord, (3) damaged peripheral neuronal paths, (4) loss of peripheral inhibition, (5) enhancement of excitatory neurotransmission in the micturition reflex pathway, (6) increased afferent input, and (7) idiopathic [2]. Decreased compliance is usually the sequelae of neurologic disease but may also result from any process that destroys the elastic or viscoelastic properties of the bladder wall.

A basic evaluation of patients presenting with overactive LUTS should include a thorough medical history, including the nature and duration of symptoms. Additional history should include any genital or sexual symptoms, prior urinary tract manipulation or surgery, gross hematuria, smoking history, and medication assessment.

Physical exam should include a digital rectal exam in men to assess prostate size, consistency, presence of nodules, and anal sphincter tone and a pelvic examination in women to assess degree of uterine or bladder prolapse, urethral hypermobility, and pelvic mass. Palpation of the bladder to rule out distension should be performed and a basic neurologic assessment of motor and sensory function of the perineum and lower extremities is warranted. Urinalysis in the form of a dipstick should be instituted with further evaluation if abnormalities are seen. Persistent overactive symptoms should be evaluated with urine cytology with consideration of cystoscopy.

A voiding diary should be completed by the patient to document the number of daily voids, the distribution of voids during the day and night, the volume voided, and fluid intake. Other parameters, when present, such as urgency and leakage of urine, should also be documented. Several validated questionnaires exist and are generally helpful to evaluate initial symptom severity and bother and the patient's response to treatment.

Treatment for these conditions is aimed at decreasing bladder activity or increasing bladder capacity generally through behavioral modifications such as timed voiding, Kegel exercises, fluid restriction, and avoidance of bladder irritants. Medication therapy with antimuscarinic drugs is added when the patient has significant bother or symptoms refractory to conservative measures.

A less common cause of urinary frequency or nocturia is *polyuria*. Polyuria refers to an increase in the volume of urine excreted on a daily basis. The etiologic

mechanisms include increased fluid intake (polydipsia, psychogenic polydipsia), exogenous or endogenous diuretics, and abnormal states of central or peripheral osmoregulation. Nocturnal polyuria refers to a disproportionate amount of urine excreted overnight compared to during the day. A decrease in nighttime antidiuretic hormone secretion is a common culprit among the elderly [31].

Increased bladder sensation or bladder pain may be the result of bladder pain syndrome/interstitial cystitis (BPS/IC). This clinical diagnosis is made after ruling out other causes of lower urinary tract discomfort. BPS/IC is defined as "an unpleasant sensation (pain, pressure, discomfort) perceived to be related to the urinary bladder, associated with lower urinary tract symptoms of more than 6 weeks duration, in the absence of infection or other identifiable cause" [32]. Therapy is aimed at increasing bladder capacity or decreasing sensory (afferent) input.

Incontinence

Urinary incontinence is defined as the involuntary loss of urine and generally occurs during the filling/storage phase of micturition. Incontinence symptoms increase with age in both men and women and consist of complaints such as stress related urinary incontinence, urgency urinary incontinence, and insensible urine loss. Incontinent urinary symptoms are described below [6].

Urinary incontinence is the complaint of involuntary loss of urine.
Stress incontinence is the complaint of involuntary loss of urine during coughing, sneezing, or physical exertion.
Urgency incontinence is the complaint of involuntary loss of urine associated with urgency.
Mixed urinary incontinence is the complaint of involuntary loss of urine during coughing, sneezing, or physical exertion (SUI) and with urgency (UUI).
Postural incontinence is the complaint of involuntary loss of urine associated with change in body position.
Nocturnal enuresis is the complaint of involuntary loss of urine during sleep.
Continuous incontinence is the compliant of continuous involuntary loss of urine.
Insensible incontinence is the complaint of urine loss without awareness.
Coital incontinence is the complaint of involuntary loss of urine with intercourse.

Etiology of Incontinence

The etiology of incontinence varies by type. The two main categories are bladder dysfunction or detrusor overactivity and urethral dysfunction or outlet underactivity. A simple classification scheme is shown in Table 10.3. Detrusor overactivity may be due to neurologic disease or may exist with or may be due to bladder outlet obstruction, inflammation, or be idiopathic. The result may be involuntary bladder

Table 10.3 Classification of the etiologies of incontinence

I. Urethral incontinence
A. Bladder dysfunction/detrusor overactivity
1. Involuntary contractions
2. Impaired compliance
B. Urethral dysfunction/outlet underactivity
1. Urethral hypermobility
2. Intrinsic sphincter deficiency
C. Functional
1. Secondary to functional disability
2. Secondary to cognitive impairment
II. Extraurethral incontinence
A. Fistula
1. Vesicovaginal
2. Ureterovaginal
3. Urethrovaginal
4. Rectourethral
B. Ectopic ureter

contractions that produce associated leakage of urine or impaired compliance producing an elevation in detrusor pressure that exceeds urethral pressure leading to incontinence. Decreased outlet resistance may result from any process that damages the innervations or structural elements of the smooth and/or striated sphincter (intrinsic sphincter deficiency (ISD)) or support of the bladder outlet in the female (urethral hypermobility). This may occur with neurologic disease, surgical or mechanical (obstetric) trauma, or aging [28]. Additionally, incontinence may be the result of functional or cognitive impairment or abnormal urinary tract communication.

SUI in the female was classically divided into two relatively discreet entities: urethral hypermobility and ISD. Hypermobility of the bladder outlet was felt to be due to poor bladder support such that during episodes of increased intra-abdominal pressure, mobility of the outlet led to loss of competence and urinary leakage. ISD is the loss of urethral competence, specifically the sphincter mechanism, such that closure pressure cannot overcome bladder pressure in certain situations [28].

These categories are considered less discrete today with the contemporary view favoring that varying degrees of each component are present in most women with SUI. Furthermore, the need for this type of discreet classification has lost its value as treatments are no longer exclusive to one entity or the other. In general, today, treatment is the same for both underlying etiologies. In theory, outlet related incontinence in the male should be similar to the female; however, hypermobility of the bladder neck and urethra has not been found as an etiology in the male. ISD in the male is felt to be the result of neurologic disease, surgical or mechanical trauma, or aging, with treatment of prostatic diseases the most common underlying cause.

UUI is described in the section on overactive LUTS above.

MUI generally results from combined deficits leading to both SUI and UUI. Combination therapy addressing each component is generally most efficacious.

Nocturnal enuresis, in isolation, is most commonly seen in children. In adults, it may be a component of the OAB syndrome and essentially due to UUI while sleeping. It can also be the result of oversedation caused by sleep aids and other psychotropic drugs. In the setting of nocturnal polyuria, nocturnal enuresis may occur due to excessive nighttime urine output. Conservative measures such as nighttime alarms to wake the patient prior to a leakage episode, fluid restriction, and treatment of lower extremity edema if present, are generally first line. When these therapies fail, antidiuretic hormone may be prescribed in order to decrease nighttime urine production.

Continuous incontinence can be the result of a urinary tract fistula, urethral erosion, or overflow incontinence. Treatment of the urinary tract fistula will often cure the patient of their incontinence; however, a high index of suspicion to make the diagnosis is necessary. Urethral erosion generally occurs in the setting of a long term indwelling catheter. Commonly, the patients affected have a neurologic condition that lead to urinary retention precipitating the initial placement of the catheter. Urethral reconstruction can be attempted in these patients, but generally bladder neck closure with diversion of urine is needed. Overflow incontinence is generally the result of bladder outlet obstruction and relief of the incontinence relies on effective management of the primary problem. For some patients, self-intermittent catheterization can ameliorate symptoms and provide a relatively noninvasive treatment option.

Insensible incontinence may occur in the neurogenic population, the elderly, or the very young. Patients report no sensation of urine loss but have the feeling of wetness. This type of incontinence can be the most challenging as it often does not respond to any of the aforementioned treatment strategies. When all else fails, options such as bladder neck closure with suprapubic tube placement, ileal chimney, and continent catheterizable reservoirs can be discussed with the patient.

Coital incontinence may occur due to SUI or UUI during intercourse or at the time of orgasm. Though the topic is controversial and little high quality data exists, a recent editorial summarizing the available evidence suggests that, "[coital incontinence] could be two separate entities: if leakage occurs at penetration, it can be almost invariably the consequence of an anatomic defect, while coital incontinence at orgasm may more frequently be related to an involuntary detrusor contraction either triggered by orgasm or by urethral instability due to sphincteric deficiency" [33]. It is uncommon for this coital incontinence to exist in isolation and generally treatment is based on concomitant symptoms and severity.

Lower Urinary Tract Changes with Age

Functioning of the lower urinary tract in an elderly individual is the result of an interaction between potential predisposing factors over which we have no or only partial control. Some of these factors involve the lower urinary tract and pelvic

floor, while others exist outside of these anatomic regions. Bladder sensation, ability to postpone, contractility, maximal urethral closure pressure, and overall mobility decrease with age, whereas detrusor overactivity, post void residual, nocturia, atrophic vaginitis, prostate size, pelvic organ prolapse, and depression all increase with age [34, 35]. Factors affecting the lower urinary tract and pelvic floor can include ischemia, ultrastructural changes, changes in innervation and receptors, and neurologic disease, as well as several others.

Ischemia and oxidative stress, related to vascular change, tobacco, diabetes, overdistension, and detrusor overactivity, result from direct damage or ischemia followed by reperfusion. Free radical release and oxidative stress can cause neurodegeneration and inflammation [36–40]. Ischemia and oxidative stress may be responsible for the progression from normal to detrusor overactivity to detrusor underactivity [41, 42]. Diabetes causes polyuria, altering glucose metabolism, which results in superoxide induced free radical formation with subsequent oxidative stress. This oxidative stress affects afferent and efferent nerves [43, 44].

In terms of cellular degeneration and ultrastructural changes, Elbadawi et al. describes a spectrum of changes from the dense band pattern (asymptomatic, normal urodynamics) to patterns associated with detrusor overactivity, detrusor underactivity, and bladder outlet obstruction; however, there is not uniform agreement regarding these observations [45–47]. Other age-related ultrastructural changes include a decline in the smooth muscle to connective tissue ratio in males and females and a loss of caveolae in the aging bladder, which could predispose to detrusor underactivity and other bladder dysfunction [48–55]. With increasing age, apoptosis occurs, which is associated with decreased striated muscle density in the rhabdosphincter, especially in women. This decreased muscle density predisposes to decreases in maximal urethral closure pressure and stress urinary incontinence [56–60]. Collagen is a major component in the urethra and its arrangement is critical to optimal functioning during bladder neck closure. Women with stress urinary incontinence, however, have a decrease in the total collagen in their skin, pelvic ligaments, and vesicovaginal fascia [61]. Furthermore, there are demonstrable abnormalities in the vaginal wall and pelvic floor supporting structures in women with pelvic organ prolapse [62]. Whether these abnormalities are causally related to aging or a result of the prolapse is uncertain.

With regards to peripheral efferent mechanisms, there is a decline in bladder autonomic innervation with aging, even in non-obstructed bladders, as well as denervation of the urethral sphincter, pelvic floor striated muscle, and anal sphincter [63–66]. This decrease in autonomic innervation may result in insufficient activation by non-uniform stimulation of detrusor or insufficient neurotransmitter release to generate uniform contractions, and may also result in a decrease in urethral resistance and pelvic floor support. Increase in ultraclose cell abutments associated with increased cellular coupling correlates with increased incidence of detrusor overactivity. This muscle degeneration would imply an overall decreased contractile force. These ultrastructural changes correlate with the combination of detrusor overactivity during filling/storage and detrusor underactivity during emptying [46]. With age, receptor number decreases; specifically, there is decreased mRNA for M_3 in

bladders, decreased beta$_3$ receptors, and increased purinergic transmission. These changes result in decreased muscarinic activation, increased atropine resistant contraction, and possibly decreased compliance [67–70]. In terms of peripheral afferent mechanisms, tissue changes associated with aging alter the biomechanical properties of the bladder such that there is a delayed desire to void resulting, after a small volume is passed, in reduction of afferent activity which leads to an early termination of detrusor contraction and decreased voiding efficiency [71, 72]. Defects in urothelial function, interstitial cells, and ganglia may alter the release of neurotransmitters and excitability of sensory nerve fibers [73]. There is sensory feedback from urethral afferents in response to flow, which normally augments detrusor pressure amplitude and duration. This likely decreases with age [74].

In regards to central mechanisms, the insular cortex, hypothalamus, periacqueductal gray, and pontine micturition center are all involved in the voiding reflex. A lesion that affects any one or more could result in detrusor underactivity, though an exact correlation between lesion site and dysfunction is not established [75]. Griffiths et al. suggested that the elderly may have underperfusion of the cerebral cortex and this could be related to bladder sensation and urge urinary incontinence [76]. White matter hyperintensities also appear with age and are structural abnormalities that may be associated with lower urinary tract disorders. In the right inferior frontal area and cingulate gyrus, these may be associated with urgency incontinence [77].

Aging is a normal process and a spectrum of changes in the lower urinary tract exists as a result of changes in the morphology, metabolism, hormonal environment, physiology, pharmacology, and cerebral control of the lower urinary tract and pelvic floor.

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Chapter 11
Behavioral Intervention for Lower Urinary Tract Symptoms in Older Adults

Alexander Skokan and Diane K. Newman

Introduction

Lower urinary tract symptoms (LUTS) and urinary incontinence (UI) are highly prevalent in the older adult population, and prevalence has been demonstrated to increase with age. Over age 60, 15 % of men and 55 % of women suffer from UI [10]. This prevalence is higher in older adults who reside in nursing homes or who are frail. Although lower urinary tract symptoms (LUTS) are "common" in older adults, they are certainly not "normal." And if not "normal", LUTS can and should be corrected. Non-invasive and effective behavioral treatments are appropriate first-line treatments in this population [12, 22].

Conservative management includes all behavioral and interventional techniques that do not incorporate pharmacologic or surgical treatment or containment devices or products. These management options aim to relieve the bothersome symptoms associated with pelvic floor functional conditions. These interventions also include lifestyle changes or self-care practices, including adjusting the intake of fluids and eliminating bladder irritants.

In the older adult, interventions such as toileting programs can be categorized as "patient-dependent" or "caregiver-dependent" [14]. Bladder training (BT) and pelvic floor muscle training (PFMT) are "patient-dependent" interventions [13, 24]. These necessitate adequate function, learning capability, and motivation of the individual. Patient-dependent interventions, including scheduled voiding, habit training (HT), and prompted voiding (PV), are useful in people with functional disabilities [14].

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Table 11.1 ICI recommendations for prompted voiding

It is uncertain whether habit retraining reduces UI in frail older persons. (Level 4)
It is uncertain whether timed voiding reduces UI in frail older persons. (Level 4)
PV is effective in the short-term treatment of daytime UI in nursing home residents and home-care clients when caregivers comply with the protocol.
PV is ineffective and should not be used for people who need the assistance of more than one person to transfer, these people should be managed with "check and change."
PV should not be continued in eligible persons who have less than a 20 % reduction in wet checks or toilet successfully less than two-thirds of the time after a three day trial; these people should be managed with "check and change."
Interventions combining toileting and exercise decrease wet checks and improve endurance in nursing home residents, including those with psychiatric disease.
Interventions combining PV, exercise, fluid and food intake interventions improve UI frequency and appropriate toileting.

Adapted from: Wagg et al. [22]

The success of these interventions is largely dependent on caregiver knowledge and motivation, rather than on the person's physical function and mental status. However, BT relies on the person's understanding of voiding habits and the ability to practice strategies to resist or delay voiding, often referred to as urgency suppression.

Behavioral treatments are strongly supported by a large body of literature and have become a primary first-line therapy for the management of LUTS in many patient populations [12]. Many of these techniques are specifically applicable to older adult patient populations, although specific consideration of patients' physical and mental functional status should drive the clinician's evaluation and the development of an appropriate individualized management plan with each patient. The 5th International Consultation on Incontinence (ICI) Committee on Incontinence in the Frail Elderly [22] made recommendations for the use of toileting programs in frail older adults (See Table 11.1)

Lifestyle Changes/Behavior Modification

In many instances, lifestyle practices can be contributing to or causing LUTS, especially in older women. Changes in certain practices, specifically weight reduction, smoking cessation, modification of fluid intake and diet, and bowel regularity, are modifiable lifestyle-related risk factors for LUTS (see Table 11.2) [13]. Lifestyle changes are aimed at improving symptoms through modifications of these practices, including the elimination of bladder irritants from the diet (see Table 11.3), fluid intake management, weight control or loss, management of bowel regularity, and smoking cessation. The ultimate goal is for the patient to adopt specific strategies that will eliminate symptoms [7]. These interventions are one component of conservative management as they improve symptoms through identification of lifestyle habits and changing a person's behavior, environment or activity that are contributing factors or triggers of LUTS [17, 24].

Table 11.2 Lifestyle changes that can improve bladder symptoms

Maintain a healthy weight	Massive weight loss (15–20 BMI points) significantly decreases UI in morbidly obese women. Moderate weight loss may be effective in decreasing UI especially if combined with exercise Weight loss in obese and morbidly should be considered a first line treatment to reduce UI prevalence
Stop smoking	Caffeine consumption may play a role in exacerbating UI. Small clinical trials do suggest that decreasing caffeine intake improves continence. Caffeine reduction may help in improving incontinence symptoms
Moderate liquid and beverage intake	Fluid intake may play a minor role in the pathogenesis of UI. Minor decrease of fluid intake by 25 % may be recommended provided baseline consumption is not less than 30 ml/kg a day
Maintain bowel regularity	There is some evidence to suggest that chronic straining may be a risk factor for the development of UI.

Adapted from: Moore et al. [11]

Table 11.3 Diet and medications. Certain food and beverages can irritate the bladder and make symptoms worse. They are

Alcoholic beverages	Citrus juices and fruits
Beer, wine	Highly spiced foods
Carbonated beverages	Sugar, honey
Milk/milk products	Corn syrup
Soft drinks with caffeine, tea, coffee even decaffeinated	Artificial sweetener – Nutrasweet (Equal)

Also some over-the-counter medications and prescription drugs contain caffeine which can worsen bladder problems such as Excedrin, Midol, Anacin, Dristan and Sinarest

As noted previously, behavioral therapies can be broadly categorized as patient-dependent interventions and caregiver-dependent interventions [18]. Patient-dependent interventions require that a patient have the functional capacity, comprehension, and motivation to institute and maintain the techniques or behavior changes that are taught. Caregiver-dependent interventions rely upon the regular presence of an in-facility or in-home caregiver, and require the compliance and motivation of the caregiver to adhere to the therapeutic intervention. Caregiver-dependent interventions can be appropriately instituted in patients with limited independent function such as those with significant neurologic deficits or those in chronic care facilities, but they do rely upon caregiver adherence. As part of the initial patient evaluation, the clinician should seek to assess a patient's physical and mental capability to adopt behavioral therapies. Also, an assessment of the patient's environment can assist in improving the toileting process (see Table 11.4). In patients with limited or no self-care abilities, who will require caregiver-dependent interventions, it is critical to ensure that the caregiver understands and can provide the support needed to implement a treatment plan.

Table 11.4 Facilitating voiding in older adults

Negotiate the voiding interval and toileting times with people who are cognitively intact to increase compliance.
Observe body language for cues about need to use the toilet in older adults who may have some cognitive impairment. Look for fidgeting, nervousness, and pacing or increased anxiety.
Try to give the person a private bathroom so someone else is never using it. Facilitate voiding by using a raised toilet seat or bedside commode to avoid having the person sitting too low.
Ensure complete bladder emptying by having the person toilet upright in a bathroom commode or a bedside commode rather than a bedpan. Having the person slowly back up to the toilet until he or she can feel the back of his or her knees touching it. After placing both hands on the commode armrests or the grab bar and edge of seat, the person lowers him- or herself slowly by bending at the knee and hip. Reversing the procedure by having the person stand up by using the grab bars and seat or commode armrests with one hand and perhaps a walker with the other. Instruct the person to keep knees bent and feet firmly on the floor when attempting to stand.
Ensure that bed height is sufficient so that, when the person sits on the edge of the bed, the feet are flat on the floor and the person can easily accomplish going from sitting to standing.
Keep a clear, unobstructed, direct walking path to the bathroom and place night-lights along the path.
Institute visual cues to indicate the location of the bathroom (e.g., put the word "toilet" on the outside of the bathroom door; show a picture of a man using a toilet).
Make sure the person can easily use the toilet (e.g., raised toilet seat, grab bars).
Make sure the person's clothing is easy to remove. Encourage the use of underwear whenever possible. Underwear serves as a reminder to stay dry and as a stimulus to use the toilet and not to wet oneself if it can be avoided.
Encourage the person to void before going to sleep.
Locate bathroom facilities when traveling, or bring a portable urinal. Choose seats in restaurants, theaters, and other such locations that are near a bathroom.
Use underpads (reusable or disposable) under bedsheets, on chairs, and in the car. Avoid use of garbage bags, rubber pads, or shower curtain liners because these may be too slippery or may irritate the skin.
Open windows or use deodorizers to cut down on odors. (A cut-up onion will absorb odors in a room without leaving its own smell. Also, an open box of baking soda will reduce odors).

Adapted from: Newman and Wein [18], Jenkins and Fultz [8]

Education: The appropriate institution and maintenance of a behavioral program relies upon patient understanding and compliance. Thus, patient education is a critical first step in addressing UI or OAB symptoms via a conservative approach. The clinician should educate the patient on relevant function and physiology of the lower urinary tract, as well as the current knowledge regarding bladder dysfunction as it applies to each patient's clinical picture. The rationale for each behavioral change should be discussed, and the clinician and patient should agree upon specific tangible therapeutic goals. Since behavioral therapies rely upon a patient's ability to change longstanding habits, it is pivotal that patients understand that behavioral therapy will be an active process and that improvement will be gradual over the course of weeks to months [9].

Weight loss: Five to ten percent of weight loss is an acceptable treatment option for morbidly obese adult women. Subak et al. [21] showed that improvement in UI

was seen when participants lost as little as 5 % from baseline weight so weight loss is recommended in clinical practice to all women who have a BMI > 30. Clinicians might suggest self-weight-loss programs such as Weight Watchers to older adults, or depending on their current BMI, might refer women to a physician- monitored weight loss program.

Fluid and dietary management: The amount of fluid ingested may be contributing to a person's LUTS and moderating fluid intake can improve LUTS. Individuals may subscribe to either a restrictive or excessive fluid intake behavior. Therefore, increasing fluid intake if a person is drinking too little and elimination of caffeinated beverages and foods can have a positive impact on bladder symptoms. Adequate fluid intake is needed to eliminate irritants from the bladder. Under-hydration may play a role in the development of urinary tract infections (UTIs) and decreases the functional capacity of the bladder. Surveys of community residing elders report self-care practices that include the self-imposed restrictions of fluids – patients develop these restrictions out of fear of UI, urinary urgency, and frequency. Adequate fluid intake is very important for older adults who already have a decrease in their total body weight and are at increased risk for dehydration.

It is common for older adults with LUTS to reduce the amount of liquids they drink in the hope that they will urinate less often. While drinking less liquid does result in less urine in the bladder, the smaller amount of urine may be more concentrated and thus irritate the bladder muscle. Highly concentrated urine (dark yellow, strong smelling) urine may cause urgency and frequency, and encourage bacteria to grow, which may lead to infection. Fluid intake should be regulated to 6–8 ounce glasses (1200–1600 cc) or 30 cc/kg body weight per day with a 1,500 mL/day minimum at designated times unless contraindicated by a medical condition (e.g. CHF). Also, consider water-based foods (e.g. jello) and other fluids. It is helpful to consume small amounts of fluids between meals so fluid intake is spread evenly throughout the daytime.

Certain ingredients in foods and fluids may affect bladder control, especially in an older adult. Therefore a goal is to identify bladder irritants in the diet and start an elimination diet to determine the effect a certain product has on bladder function. If an irritant is identified, the goal then is to decrease or eliminate it. Caffeine is a known bladder muscle irritant, acts as a diuretic, and is a central nervous system irritant. Caffeine is found in tea, coffee, colas, and other drinks. Foods that contain chocolate also contain caffeine. It is recommended that patients consume no more than 2 cups of caffeinated drinks per day or switch to caffeine-free products. Nutritional supplements, puddings and cakes that contain cocoa, which contains caffeine, are favorite foods and daily staples in nursing homes. Alcohol with dinner may be a contributing factor for nocturia. Anecdotal evidence suggests that eliminating dietary factors such as artificial sweeteners (aspartame) and certain foods (e.g. highly spiced foods, citrus juice, ice and tomato-based products) may play a role in continence. Patients also need to read product labels. Herbal teas which are felt to be more "natural" usually contain caffeine unless listed otherwise. Patients seem to think that iced tea has less caffeine than hot tea. In many patients, who ingest large quantities, total elimination may be unrealistic. It is recommended that

patients with incontinence and OAB avoid excessive caffeine intake (e.g. no more than 200 mg/day, 2 cups).

Management of nighttime LUTs: In a geriatric population, there appears to be a strong relationship between evening fluid intake, nocturia, and nocturnal voided volume. Aging causes an increase in nocturia, defined as the number of voids recorded from the time the individual goes to bed with the intention of going to sleep, to the time the individual wakes with the intention of rising Nocturia is an average of less than 2 nocturnal voids per night.

Nocturia can be diagnosed as nocturnal polyuria (NP) which causes the largest amount of urine production to occur at rest while the person is supine. Chronic medical conditions such as heart failure, venous stasis with peripheral edema, hypoglycemia and excess urine output, obstructive sleep apnea, and diuretics as well as evening/nighttime fluid consumption are causes of NP.

During the night, there is a lower level of physical activity and body fluid moves more quickly from one part of the body to another causing an increase in the amount of urine in the bladder.

Timing of fluid intake may be important in persons who have problems with nocturia. Older adults who experience nocturia and/or NP more than twice a night, or who experience nocturnal enuresis (UI while asleep) may benefit from fluid restriction in the evening (e.g., stop at 7 p.m. or at least 2–3 h before bedtime). These individuals can maintain adequate fluid intake by drinking the bulk of their liquids during the day hours. They may also benefit from elimination of caffeine in the evening. If peripheral edema is present, elevation of the extremities on a stool or recliner during the day (e.g., early afternoon) can stimulate natural diuresis and limit the amount of urine production and voiding during the night.

Bowel regularity: Chronic constipation and straining during defecation can contribute to LUTS and pelvic organ prolapse in women. The close proximity of the bladder and urethra to the rectum and their similar innervations make it likely that there are reciprocal effects between the two systems. Constipation is defined as having less than 3 stools per week. Usually a patient's definition of constipation is considerably broader, however, and includes straining during defecation, painful defecation, vaginal splinting to aid defecation, dry hard stools, small stools, and incomplete or infrequent stool evacuation. Studies of severely constipated women who have strained during defecation over a prolonged period have demonstrated changes in pelvic floor neurological function.

As there is data to suggest that chronic constipation and straining may be a risk factor for the development of LUTS, especially in women, self-care practices that promote bowel regularity should be an integral part of any treatment care plan. Suggestions to reduce constipation include the addition of fiber to the diet, increased fluid intake, regular exercise, external stimulation, and establishment of a routine defecation schedule. Improved bowel function can also be achieved by determining a timetable for bowel evacuation so that the patient can take advantage of the urge to defecate. The schedule should be determined by the patient's bowel elimination pattern and previous time pattern for defecation. The patient should be taught never to ignore the "call to stool", the feeling that the bowel needs to be emptied.

Table 11.5 Contribution and solutions to UI in patient with cognitive impairment

Cognitive effects	
Contributing factors	Solutions
Geographic disorientation (does not know location of toilet even in own home, if door bathroom door is shut "doesn't exist" behind it). Agnosia (inability to recognize objects, persons, sounds, shapes, or smells, cannot read words, usual pictorial signs of man or woman that depicts a toilet may be meaningless) Aphasia (inability to produce and/or comprehend language). Visuospatial deficit (inability to visually perceive spatial relationships among objects e.g. men stand too far away from toilet bowl and have an inaccurate aim)	Remind or take to toilet at least every 3 h Place picture of toilet on the door Make the door of the bathroom a different color Leave door of bathroom open so toilet can be seen Write out consistent and clear instructions on voiding and read to patient to prompt voiding Gently steer male patient forward, give help to aim penis into toilet bowl Consider having male patient sit down
Behavioral problems	
Contributing factors	Solutions
Active – disinhibition, restlessness, anxiety (e.g. distaste, even phobia of using communal toilets) Passive – apathy, depression, overdependency, attention-seeking (may be caused by embarrassment over UI and FI problems)	Approach the patient with a calm and reassuring attitude Replace white toilet seat with a colored one (these could be colored "disposable" seat covers) Maintain continuity and familiarity of caregiver staff Respect patient's dignity and be aware of personal preferences
Mobility problems	
Contributing factors	Solutions
Impaired mobility, dexterity and clothing manipulation Impaired vision (may not be able to see toilet seat) Apraxia (loss of the ability to execute or carry out learned purposeful movements)	Simplify clothing: sweatpants, elasticized waistbands Replace white toilet seat with a colored one (these could be colored "disposable" seat covers)

Adapted from: Newman and Wein [18], Jenkins and Fultz [8]

Toileting Programs

The simplest methods to pursue management of urinary incontinence and OAB in patients with limited independent functioning is through toileting programs. These plans are best applied to patients with mobility or cognitive impairments, but who do have the capability to participate in a toileting regimen. Determining the barriers that older patients find to toileting and identifying solutions will increase the success of these programs (see Table 11.5). Toileting programs can include timed voiding, prompted voiding, or habit training.

Timed voiding: Timed voiding (TV), also referred to as habit training, is scheduled toileting at regular intervals on a planned basis to match the person's voiding

DAY 1					
Time	**Trips to bathroom** How much urine did you pass (in oz)?	**Did you feel a strong urge to go?** (yes, no)	**Urine Leakage**	**Circumstances of Urine Leakage**	**Drinks** What kind and how much? 1 glass = 4 oz 1 cup = 8 oz
6:00 a.m. - Awake	6 oz	yes	✓	Getting out of bed rushing to bathroom	½ glass of water
6:30 a.m.	3 oz	yes			1 ½ cups of coffee,
8:30 a.m.	5 oz	yes			1 cup of coffee
10 a.m.	7 oz	yes	✓		½ glass of water
12 p.m.					8 oz of soda, 1 glass of milk, 1 glass of water
12:30 p.m.	4 oz	yes		Running water, washing hands	
2:30 p.m.	7 oz				½ glass of water
4:30 p.m.			✓	Coming home from shopping	1 cup of tea
5 p.m.	4 oz				2 glasses of water
7 p.m.	8 oz	yes	✓	On the way to bathroom	1 glass of cola
8 p.m.	4 oz				2 glasses of wine
10 p.m.-to bed	4 oz				
12 a.m.	5 oz	yes			
2 a.m.	don't know				
3:30 a.m.	10 oz	yes			½ glass of water
5 a.m.	don't know				
TOTAL	**10 daytime voids/ 4 nighttime voids Volume 67 oz+/2010 ml+**	**8 urgency episodes**	**4 incontinence episodes**		**72 oz cups/glasses (2160 ml)**

Fig. 11.1 Bladder diary

habits or needs. TV seeks to develop a fixed voiding schedule during the day, which is usually suspended overnight. Patients void immediately after awakening, then at a fixed interval (e.g. every 3–4 h) throughout the day and once immediately prior to going to bed at night. In TV, no rehabilitation of the bladder is involved. The individual is a passive participant; there are no attempts to assist the individual in delaying voiding or resisting the urge to void. The goal is to pre-empt an incontinence episode. The following are steps recommended for implementing TV:

- Keep a bladder diary for at least 3-days to ascertain a voiding and incontinence pattern. Based on the observed pattern, a toileting interval is established, usually every 2–3 h or based on events (e.g., after breakfast and after lunch). Figure 11.1 is an example of a completed 1-day diary.
- In establishing the interval between voidings, one could negotiate the interval with a caregiver or cognitively intact patient to increase compliance.

- Encourage the person to void in the toilet, commode, or bedpan/urinal, whichever is most suitable, even when incontinence episodes occur, to assure complete bladder emptying.
- Combining OAB drug therapy (antimuscarinics/anticholinergics) with scheduled toileting may provide the best outcome in decreasing UI.

Prompted voiding: In patients with physical or cognitive disabilities that would limit or preclude the use of patient-driven treatments, interventions such as PV that rely upon the involvement of caregivers can be of benefit in the management of UI. This is especially relevant in the elderly population, which includes a large subset of individuals in chronic assisted living facilities or with disabilities requiring long-term in-home assisted care. This method is based upon timely reminders to toilet and positive reinforcement from caregivers to maintain continence [16]. The intervention has been used successfully to treat UI in acute and long-term care facilities, as well as in home care settings [4, 19]. Three primary behaviors that the caregiver uses each time PV is initiated:

- Monitoring: determining voiding interval/pattern based on individual's bladder diary.
- Prompting: is antecedent to toileting assistance from the caregiver. Prompting includes reminding the person to use the toilet as well as encouraging maintenance of bladder control between PV sessions.
- Praising or encouragement: is the consequence to the individual's success with maintaining bladder control. Praising, or feedback, is the positive reinforcing of dryness and appropriate toileting.

Older adults who would be excluded from these programs are persons with mobility impairment necessitating a mechanical or multiple person transfer, those terminally ill, comatose, or severely behaviorally disturbed residents. Such patients are generally not candidates for a prompted voiding trial.

Prior to implementing a PV program, conducting a 3-day trial to determine if that person is appropriate for this type of toileting program may be helpful. Predictors of a good response include those who:

- Respond to prompts when toileting
- Void an adequate volume of urine (at least 150–200 mL or 5–7 ounces)
- Have appropriate number of voids (voids at least 50 % of the time into a toileting receptacle)
- Have incontinence frequencies <4 episodes in 12 h (baseline incontinence rate)
- Have normal PVR urine volume (<150–200 mL or 5–7 ounces)

There are several strategies that can be used to assist an older adult in successful voiding (see Tables 11.3 and 11.4. Ensure an appropriate toileting environment by providing privacy during toileting and placing toilet tissue. Do not rush the person but allow them to sit on the toilet or commode for about 15 min. A shorter time is too rushed and more time defeats the purpose.

Retraining Behavioral Programs

Bladder training involves retraining to restore normal bladder function by gradually increasing the intervals between voiding in an attempt to correct urinary frequency and eventually diminish urgency. Bladder training is a toileting program that involves education and behavioral training to suppress urgency, so the person must be actively involved. Unlike scheduled toileting programs, in which the voiding schedule is adjusted to the needs of the individual, BT encourages expanded voiding intervals through urge suppression.

Bladder training is used for highly motivated adult patients without cognitive or physical impairments. The goal of BT is to restore normal bladder function through a process of patient education along with a mandatory or self-adjustable voiding regimen that gradually increases the time interval between voids. How BT achieves its effects on improving lower urinary tract symptoms is unclear. One hypothesis is that it strengthens the brain's control over bladder sensations and urethral closure [5, 6]. An alternative hypothesis is that individuals change their behavior in ways that increase the 'reserve capacity' of the lower urinary tract as they become more knowledgeable of circumstances that cause bladder leakage [6, 25].

Bladder training offers the advantages of being simple, relatively inexpensive, and free from unpleasant side-effects [23]. This makes it particularly attractive for use in older adults, particularly those with many comorbidities who are already on multiple drug regimens and for whom OAB drug therapy, because of its anticholinergic properties, would place them at higher risk for adverse drug effects.

- Determine voiding pattern from a 3-day bladder diary.
- When usual voiding times have been established, progressively lengthen the times or intervals between voids. Usually, BT starts at hourly intervals and gradually lengthens to every 2–3 h. As the bladder capacity increases, voiding intervals increase and urgency decreases.
- Teach the individual that "urgency" is the sudden need to void immediately that may result in urine leakage. Urgency follows a wave pattern; it starts, grows in intensity until it peaks, and then subsides and stops until the next wave begins (see Fig. 11.2).
- Teach behavioral training that includes urge suppression techniques. The key to controlling the urinary urge is not to respond by rushing to the bathroom. Rushing causes movement, which jiggles the bladder, and in turn increases the urge sensation. The person should wait until the urgency subsides, then walks slowly to the bathroom.
- Strategies to help with controlling urges include:
  - Concentrating on another body sensation such as deep breathing. Sitting down and taking five slow, deep breaths, concentrating on breathing. Visualizing the air moving in and out of the lungs, rather than focusing on the bladder urgency sensation, promotes bladder relaxation.
  - Performing five quick, strong pelvic floor muscle contractions.

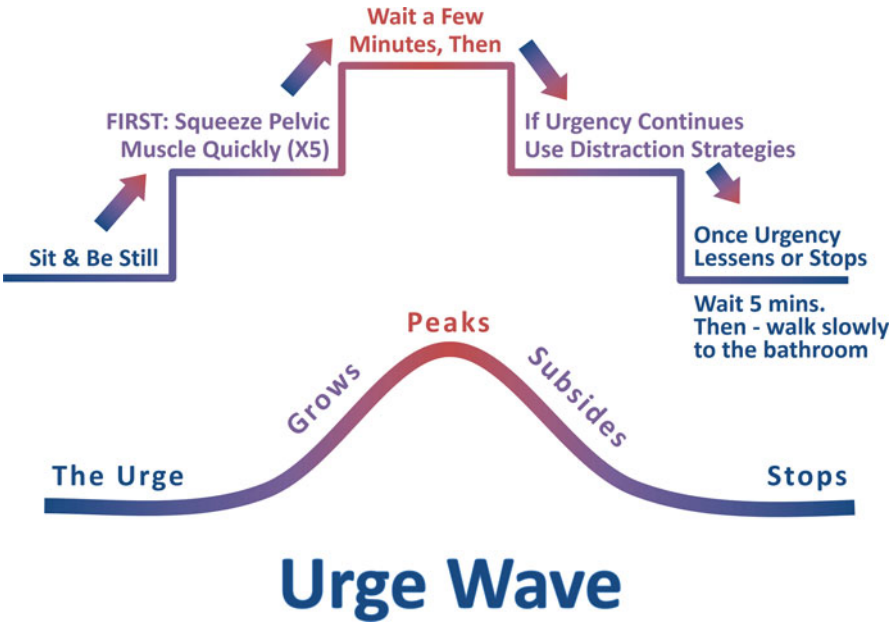

Fig. 11.2 Steps to control urgency

  - Using mental distraction strategies such as concentrating on an activity (e.g. counting backwards from 100 by 7's, or reciting the words of a favorite song or nursery rhyme).

- After the urgency goes away, the individual should walk unhurriedly to the bathroom to void. Urgency is further compromised by the action of rushing to the bathroom and rushing can cause a fall in this at-risk population. Becoming anxious over the possibility of not reaching the toilet before urine leakage occurs can also be a trigger for worsening urgency.
- Once control is gained over urgency, fewer episodes of urgency will occur, allowing the older adult to delay voiding for longer periods of time and to achieve a more normal voiding pattern.

When BT is combined with PFMT for mixed UI, a high level of evidence was found that indicates significant improvement in urinary incontinence [20].

Pelvic floor muscle training: Strengthening the pelvic floor muscle through exercising has a central role in the conservative management of UI and OAB. There is a strong body of literature supporting the use of PFMT in females, and while less data exists regarding its use in men it has still been proven to be beneficial in this population, especially following prostate cancer surgery [12]. The rationale underlying the use of PFMT is that regular voluntary contraction and relaxation of the pelvic floor muscles (PFM) can strengthen and "train" this muscle group. During activities that increase abdominal pressure or during episodes of urgency, the patient will be able

to initiate a voluntary PFM contraction in order to mitigate bothersome symptoms. Pelvic floor muscle training is an approach that is likely best implemented in a supervised setting, with regular clinician visits to aid with patient adherence and to ensure that patients identify and continue to use the correct muscles in their daily regimens. PFMT is a stepwise program that involves: (1) teaching the patient to identify and contract/relax the PFM, (2) developing a schedule for regular PFM exercise to improve strength and PFM control, and (3) instituting the developed skills to contract or relax the PFM at times of symptom triggers.

Low-tone PFM dysfunction (atrophy and weakness of the PFM with an inability to isolate and contract this muscle group) can occur with denervation of the pelvic floor – this is thought to contribute to some cases of UI and POP [17]. High-tone PFM dysfunction (spastic PFM with difficulty isolating and relaxing this muscle group) is thought to occur more often in patients with chronic pelvic pain syndromes or OAB.

To start, patients will need to isolate the correct muscle. This begins with an assessment of the PFM during digital pelvic or rectal examination. The female patient can learn to pull in her vagina and both males and females can learn to pull in their anus or rectum (like when a person is trying to hold back the passing of flatus). Contraction and relaxation of the muscle is for equal periods of time. These exercises can be done anytime or anywhere, since the muscle is internal and no one can see the patient performing the exercises. For these exercises to be effective, they must be taught properly and reinforced frequently. They require an individual's understanding, cooperation, compliance and participation. Patients usually start with 5 s contractions and slowly, over several weeks, increase to 10 s contractions. About 20 exercises in the morning and 20 in the afternoon are recommended. After 2–4 weeks of consistent daily exercise, fewer incontinence episodes should be noticed. Optimal improvement may take 4–6 months of consistent exercises.

- Track incontinence, voiding frequency and urgency on the bladder diary to help the patient identify progress and provide encouragement to continue practicing.
- In addition to doing the prescribed set of PFM exercises, the patient should learn to contract the muscle just before and throughout the activity that triggers episodes of incontinence, for example:
  - Begin a contraction about 1 s before initiating a hard cough and maintain the contraction throughout the cough.
  - For prolonged activities (e.g., walking to the bathroom), tighten the muscle during the entire activity.

Biofeedback may be considered as an adjunct in the implementation of PFMT [16]. Biofeedback uses monitors to provide either visual or auditory feedback that can assist patients with identifying and functionally isolating the PFM. Feedback from the clinician during a manual palpation PFM exam acts similar to biofeedback, but is reliant upon the examiner to provide cues to the patient.

There have been a limited number of studies investigating the use of PFMT as an adjunct in addition to another modality of active treatment. While there has not been a demonstrated statistically significant improvement in UI symptoms or QOL, a recent

Cochrane analysis of these studies rated the quality of available evidence as low or very low [2]. A number of included trials demonstrated a trend toward improvement in symptom control with behavioral, mechanical, or pharmacologic therapies plus PFMT versus the same therapies alone.

There is debate regarding whether initiation of PFMT preoperatively before radical prostatectomy or postoperatively at the time of catheter removal may prove better in expediting the return to continence in the majority of men [15]. A randomized controlled trial by Centemero et al demonstrated significantly higher continence rates in men who started PFMT preoperatively than in those who initiated PFMT only after catheter removal [3].

The long-term impact of PFMT on improving continence rates in men after radical prostatectomy remains less clear. A Cochrane analysis [1] reviewing the use of PMFT versus no therapy for the treatment of postprostatectomy incontinence did not find a statistically significant difference in continence rates at 12 months postoperatively (relative risk of persistent incontinence 0.85, 95 % confidence interval 0.6–1.22). PFMT may not help men destined to have prolonged incontinence, but this therapy could still help to expedite a return to continence for those men who would eventually recover from postoperative UI. Notably, the same Cochrane analysis found that PFMT with or without biofeedback showed significant benefit in preventing new urinary incontinence after prostatectomy (relative risk of incontinence at 12 months postoperatively 0.32, 95 % confidence interval 0.2–0.51)

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Chapter 12
Geriatric Sexuality

Hailiu Yang, Christina Ho, Philip T. Zhao, Daniel Su, and Allen D. Seftel

Abbreviations

5-ARI	5 alpha reductase inhibitors
ADAM	Androgen Deficiency in the Aging Male
AE	Adverse events
AIDS	Acquired Immune Deficiency Syndrome
AMS	Aging male symptoms
AUA	American urologic association
BID	Twice a day
BMD	Bone mass density
BSO	Bilateral salphingoophrectomy
CGI	Clinician global impression
CGIC	Clinical global impression of change
CVA	Cerebrovascular accident
DHEA	Dehydroepiandrosterone
DVT	Deep vein thrombosis
ED	Erectile dysfunction
ERT	Estrogen replacement therapy

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FDA	Food and drug administration
FSDS R	Female Sexual Distress Scale-Revised
FSFI	Female Sexual Function Index
FSH	Follicle stimulating hormone
HIV	Human immunodeficiency virus
HSDD	Hypoactive sexual desire disorder
IELT	Intravaginal ejaculatory latency time
IIEF	International Index of Erectile Function
IPSS	International prostate symptom score
LUTS	Lower urinary tract symptoms
MCID	Minimal clinically important difference
MI	Myocardial infarction
OR	Odds ratio
OSA	Obstructive sleep apnea
PDE5-I	Phosphodiesterase 5 inhibitors
PDQ	Psychosexual daily questionnaire
PE	Premature ejaculation
PEP	Premature ejaculation profile
PGI	Patient global impression
PSA	Prostatic specific antigen
QHS	Every hour of sleep
Qmax	Maximum urinary flow rate
RCTS	Randomized control trials
RR	Relative risk
RR	Risk ratio
SD	Sexual desire domain
SERM	Selective estrogen receptor modulator
SMD	Standard mean difference
SS	Symptom score
SSE	Satisfying sexual episodes
T	Testosterone
TAH	Total abdominal hysterectomy
TG	Triglyceride
UTI	Urinary tract infection
VA	Veterans affair

Introduction

> Fifty marks the beginning of the best years of our lives, including the best sex of our lives.
>
> – Dr. Christiane Northrup

The older population of the United States, focusing upon persons aged 65 years or beyond numbered 39.6 million in 2009 and is expected to rise significantly to

almost 55 million by 2020 [59]. Knowledge regarding sexuality amongst older Americans is limited as it encompasses aspects including function, behavioral activity, partnership attitudes, and general health [114]. As men and women grow older, they are susceptible to physiologic changes, medical comorbidities, and social stressors that can affect sexual health. Despite this fact, numerous studies show that a substantial number of older people engage in intercourse and sexual behavior even into their eighth and ninth decade of life. A major population-based survey examining sexual activity elderly [116] found that the frequency of sexual activity in people up to 74 years of age in the U.S. was similar to that reported in adults 18–59 in the 1992 National Health and Social Life Survey [102], a probability sample study of sexual behavior in a demographically representative cohort of US adults. According to in Lindau et al., about 26 % of patients age 75–85 were sexually active within the past year despite a significantly higher ratio (≈50 %) of bothersome sexual problems [116]. Numerous studies further substantiate the high prevalence of sexual activity in the elderly population in the U.S. and worldwide [104, 144, 163].

An unsettling fact is that an elderly patient's sexual dysfunction is rarely mentioned in the healthcare setting. Population-based surveys have consistently shown a gap between patients who have discussions with their healthcare provider about sexual dysfunctions and patients who want such a discussion. Lindau et al. showed that despite high rates of sexual dysfunction in the elderly, only 38 % of men and 22 % of females have had discussions about sex with a physician since age 50. In a population-based survey [104], 11.5 % of men and 15 % of women have had a discussion with their physician about sexual difficulties in the past 3 years; 59.2 % of men and 54 % of women believed that doctors should routinely inquire about these problems. A major contributor to this barrier to adequate diagnosis and treatment of sexual conditions in older adults is the perpetual myths regarding sex in aging individuals. Common myths include the fact that erectile dysfunction (ED) is a normal part of aging, that old people do not have sexual desires or capabilities, and that the elderly are too frail to attempt intercourse or that sex in this age group is perverse [156]. In addition, the media has perpetuated some of these stereotypes of "dirty old men" and portrayed the elderly in a negative light when it comes to their sexuality [156]. These social stigmata have no basis in reality and do a disservice not only to the large portion of the country's population who are elderly but also to the medical professionals who treat older patients.

Contrary to the stereotypes mentioned above, sexuality is a marker of good health and emotional well-being in the elderly. Numerous medical conditions can lead to decreased sexual function and satisfaction either through direct medical pathologies, pain and weakness, or the anxiety [117]. Lindau et al. [116] showed that decreased self-rated health status was correlated with the likelihood of sexual activity in past 12 months in men (odds ratio [OR] = 0.53 good vs. very good/excellent and OR = 0.21 for poor/fair vs. very good/excellent) and females (OR = 0.70 good vs. very good/excellent and OR = 0.36 for poor/fair vs. very good/excellent). Physical health problems of self or partner was cited as the most common reason for abstinence (40–65 %). Higher sexual satisfaction also leads to better functional sta-

tus and quality of life. Laumann et al. [102] found in a population-based survey that sexual problems were significantly associated with low physical satisfaction, low emotional satisfaction, and low general happiness. Matthias et al. [124] showed that higher sexual satisfaction and activity was associated with higher scores in numerous indicators of activity and socio-psychological health. For these reasons, sexuality is an important aspect of the well-being of our country's older population and should not be discouraged. In order to build a healthy society and integrate our increasingly older population, the public and healthcare community should be open-minded and tolerant of its aging citizens in regards to their sexuality.

In this chapter, we hope to illustrate the complex and multi-factorial nature of sexuality in the elderly population and demonstrate the need for an open, individualized discussion to address each patient's specific concerns. We also highlight the current knowledge regarding the pathophysiology, clinical manifestation, and evidence for treatment of these problems in the geriatric population.

Male and Female Sexuality

As people age, they develop a wide variety of problems involving their sexuality, some of which are gender specific, some of which are universal.

The description of the incidence and prevalence of sexuality of the aging population is relatively recent. This barriers to accumulating these data include the sensitivity of the subject matter, the difficulties in conducting what may potentially be embarrassing interviews, the poor response rate from surveys, and self-reporting biases. In addition to studies discussed above by the Laumann et al. [102] and Lindau et al. [116], The Global Study of Sexual Attitudes and Behaviors further characterizes sexual dysfunction in the elderly population [103]. This large, well-designed multinational study collected data from 27,500 men and women aged 40–80 years of age using standardized questionnaires. The authors found that more than 80 % of men and 65 % of women had sexual intercourse during the past year. The most common sexual dysfunctions for men were early ejaculation (14 %) and erectile dysfunction (10 %). For women, the lack of sexual desire (21 %), inability to research organism (16 %) and inadequate lubrication (16 %) were most common sexual problems. Overall, 28 % of men and 39 % of women were affected by at least one sexual dysfunction. This study found that sexual desire and activity are in fact widespread amongst the elderly population; the prevalence of sexual dysfunction was quite high and tends to increase with age.

There exist significant emotional and life -cycle disparities between men and women as they grow older. Older men generally are more prone to be involved in a relationship than their female counterparts; a study shows that 78 % of men aged 75–85 were in a spousal or sexual relationship compared to 40 % of the women in the same age group [116]. This wide gap can be attributed to several factors including the age structure. Women were also more likely to rate sex as an unimportant

part of life and relationships versus men. A multinational survey of people aged 40–80 years of age shows that women prioritize cognitive and emotional aspects of sexuality as well as general happiness as a more important component of subjective sexual well -being [103]. Women also reported a higher proportion of lack of pleasure with sex. Despite the fact that bothersome sexual problems effect men and women equally, women were less likely than men to discuss these problems with their physicians [146]. Issues include patient unwillingness to initiate discussion, poor general communication with the doctor, sex and age differences between the patient and physician, and negative social attitudes about women's sexuality especially at older age [66, 115].

Changes in Sexual Cycle with Age

The four stages of sexual response cycle change as people grow older – excitement, plateau, orgasm, and resolution [62, 85]. Excitement depends on a multitude of visual, olfactory, auditory, and memory stimuli. Plateau is defined as the maintenance and intensification of arousal. Orgasm involves the rhythmic muscular contractions typical of climax. Resolution is the state of relaxation after orgasm.

These stages change dramatically as men and women age and they impact sexuality at every level [40]. For women, there is elongation of the excitement and plateau stages as they age. This is associated with increased time to attain sufficient vaginal lubrication, as there is a marked decrease in production of lubricants. Orgasmic contractions decrease in quantity and intensity, as there is atrophy of the vaginal mucosa, reduced elasticity and less muscle tone. There is also a sharp decrease in the length of the resolution stage. Anatomically, there is significant atrophy of the vaginal tissues, decreased vaginal canal length and width, loss of vulvar tissue, and decrease in clitoris size. Estrogen and testosterone levels fall sharply and play a dominant role in changes in female sexual function after menopause [33, 40]. In some women after menopause, the loss of reproductive capacity either diminishes interest in sexual intercourse or increases the eagerness to engage in sexual activities because the fear of pregnancy is gone [40].

In the elderly male, all four stages of sexual response decrease as men age [84]. More time is required for penile stimulation in order to obtain and maintain a sufficient erection to engage in sex. There is a prolongation of the plateau phase with a shorter transition from orgasm to ejaculation. Orgasms become weaker with shorter intervals and smaller contractions. There is also a significant reduction in the amount of semen volume compared with younger men [141]. Penile detumescence occurs more frequently and rapidly in the resolution phase and there is a prolonged refractory period between erections [123]. Of course, all of these changes occur in conjunction with decreasing levels of testosterone, which is a primary driver of sexual desire and perhaps sexual function in males.

Assessment of Sexual Dysfunction in Aging Men and Women

Sexual Medicine History and Physical Examination

The office evaluation consists of a series of direct questions about the nature of the sexual dysfunction complaint, as delineated in Table 12.1 (adapted from [170]). The interview should take place in a quiet room, in a nonjudgmental fashion. These men and women are embarrassed and often need reassurance that this topic is acceptable

Table 12.1 Series of questions a clinician should ask to characterize the nature of sexual dysfunction

Characterize the sexual dysfunction for males: What type of sexual problem does the patient complain of?
Does he have ED, low desire, premature ejaculation, delayed ejaculation
If so, how long has he had the problem?
When was the last time he had intercourse?
When was the last time he had any sexual activity?
Does the sexual problem bother him?
Does the sexual problem bother his partner?
Did the problem arise suddenly (psychogenic), or has it arisen gradually?
Did the problem start when he started a new medication?
Does the problem occur with his partner only, or does it also occur without his partner, for example, with masturbation?
Does the problem occur because he has no partner or an uninterested partner?
Does he have a partner outside of his main relationship?
Can he get an erection? If so, is it firm enough for penetration?
Can he maintain the erection for intercourse?
Does he have a problem with sexual desire?
How long has he lost sexual desire?
Has he lost sexual desire with all partners?
Has he lost desire under all circumstances?
Has he lost desire because he cannot get or maintain an erection?
Has he lost desire because his partner has lost desire?
Does the patient complain of other associated symptoms, such as being tired, loss of stamina, loss of strength, loss of muscle mass, loss of muscle tone, recent weight gain, fatigue, or sleep issues?
Is the patient depressed?
Does he have a problem with ejaculation?
What type of ejaculation problem does the patient complain of?
When did the problem start?
Is the problem bothersome to the patient?
Is the problem bothersome to the partner?
Does the problem occur under all circumstances?

Adapted with permission from Seftel et al. [170]

to discuss. The questions should be asked in a gentile manner, avoiding any gestures or posturing that might be misconstrued. While, it is worthwhile to for the patient to bring his/her partner into the office for further history, queries and discussion at the time of the visit, it should be recognized that this is very uncommon. A similar interview paradigm should be employed for the female patient with sexual dysfunction [35].

Suggested laboratory work for the male patient presenting with sexual dysfunction is offered in Table 12.2 [170]. Clinician judgment is used here. For example, if the patient is a known diabetic, a serum glucose many not be needed. Thus, these tests are obtained based upon the clinical scenario.

The objective assessment of male and female sexual function has been challenging. Most regulatory agencies have allowed self-reported, validated instruments to be used as surrogate markers for sexual activity endpoints. Many instruments have been published that meet or fulfill these needs. It is important to bear in mind that to our knowledge, these instruments are not specific to the aging male or female population, but rather are for general use. Data for the aging male and female is extrapolated from these instruments.

Male Sexual Function Assessments

The instrument that has been used most often used to capture the severity of general male sexual function, and male erectile function in specific is the International Index of Erectile Function (IIEF, Table 12.3). This instrument was developed as an

Table 12.2 List of lab tests frequently performed for patients with sexual dysfunction

Laboratory tests for patients with sexual dysfunction
Fasting lipid
Fasting glucose
TT and FT (morning testing preferred)
PSA: mandatory if considering testosterone supplementation
Optional laboratory tests
Prolactin
Creatinine
Estradiol
Thyroid-stimulating hormone (TSH)
Follicle-stimulating hormone (FSH)
Luteinizing hormone (LH)
Dehydroepiandrosterone (DHEA)
25-hydroxyvitamin D level
SHBG
Albumin

Adapted with permission from Seftel et al. [170]

Table 12.3 International Index of Erectile Function (IIEF) questionnaire

IIEF Questionnaire
Instructions: These questions ask about the effects your erection problems have had on your sex life, over the past 4 weeks. Please answer the following questions as honestly and clearly as possible. In answering these questions, the following definitions apply
Definitions:
Sexual activity includes intercourse, *caressing*, *foreplay and masturbation*
Sexual intercourse is defined as vaginal penetration of the partner (*you entered the partner*)
Sexual stimulation includes situations like foreplay with a partner, *looking at erotic pictures*, etc.
Ejaculate is defined as the ejection of semen from the penis (*or the feeling of this*)
Mark Only one circle per question:
1. Over the past 4 weeks, how often were you able to get an erection during sexual activity?
1 Almost always or always
2 Most times (much more than half the time)
3 Sometimes (about half the time)
4 A few times (much less than half the time)
5 Almost never or never
0 No sexual activity
2. Over the past 4 weeks, when you had erections with sexual stimulation, how often were your erections hard enough for penetration?
5 Almost always or always
4 Most times (much more than half the time)
3 Sometimes (about half the time)
2 A few times (much less than half the time)
1 Almost never or never
0 No sexual stimulation
Questions 3, 4 and 5 will ask about erections you may have had during sexual intercourse.
3. Over the past 4 weeks, when you attempted sexual intercourse, how often were you able to penetrate (enter) your partner?
5 Almost always or always
4 Most times (much more than half the time)
3 Sometimes (about half the time)
2 A few times (much less than half the time)
1 Almost never or never
0 Did not attempt intercourse
4. Over the past 4 weeks, during sexual intercourse, how often were you able to maintain your erection after you had penetrated (entered) your partner?
5 Almost always or always
4 Most times (much more than half the time)
3 Sometimes (about half the time)
2 A few times (much less than half the time)
1 Almost never or never
0 Did not attempt intercourse

5. Over the past 4 weeks, during sexual intercourse, how difficult was it to maintain your erection to completion of intercourse?
0 Did not attempt intercourse
1 Almost always or always
2 Most times (much more than half the time)
3 Sometimes (about half the time) 0 A few times (much less than half the time)
4 A few times
5 Almost never or never
6. Over the past 4 weeks, how many times have you attempted sexual intercourse?
0 No attempts
1 1–2 attempts
2 3–4 attempts
3 5–6 attempts
4 7–10 attempts
5 11 or more attempts
7. Over the past 4 weeks, when you attempted sexual intercourse how often was it satisfactory for you?
5 Almost always or always
4 Most times (much more than half the time)
3 Sometimes (about half the time)
2 A few times (much less than half the time)
1 Almost never or never
0 Did not attempt intercourse
8. Over the past 4 weeks, how much have you enjoyed sexual intercourse?
5 Very highly enjoyable
4 Highly enjoyable
3 Fairly enjoyable
2 Not very enjoyable
1 Not enjoyable
0 No intercourse
9. Over the past 4 weeks, when you had sexual stimulation or intercourse how often did you ejaculate?
5 Almost always or always
4 Most times (more than half the time)
3 Sometimes (about half the time)
2 A few times (much less than half the time)
1 Almost never or never
0 Did not attempt intercourse
10. Over the past 4 weeks, when you had sexual stimulation or intercourse how often did you have the feeling of orgasm or climax (with or without ejaculation)?
5 Almost always or always
4 Most times (much more than half the time)
3 Sometimes (about half the time)

(continued)

Table 12.3 (continued)

2 A few times (much less than half the time)
1 Almost never or never
0 No sexual stimulation or intercourse
Questions 11 and 12 ask about sexual desire. Let's define sexual desire as a feeling that may include wanting to have a sexual experience (for example, masturbation or intercourse), thinking about having sex or feeling frustrated due to a lack of sex.
11. Over the past 4 weeks, how often have you felt sexual desire?
5 Almost always or always
4 Most times (much more than half the time)
3 Sometimes (about half the time)
2 A few times (much less than half the time)
1 Almost never or never
12. Over the past 4 weeks, how would you rate your level of sexual desire?
5 Very high
4 High
3 Moderate
2 Low
1 Very low or none at all
13. Over the past 4 weeks, how satisfied have you been with you overall sex life?
5 Very satisfied
4 Moderately satisfied
3 About equally satisfied and dissatisfied
2 Moderately dissatisfied
1 Very dissatisfied
14. Over the past 4 weeks, how satisfied have you been with your sexual relationship with your partner?
5 Very satisfied
4 Moderately satisfied
3 About equally satisfied and dissatisfied
2 Moderately dissatisfied
1 Very dissatisfied
15. Over the past 4 weeks, how do you rate your confidence that you can get and keep your **erection**?
5 Very high
4 High
3 Moderate
2 Low
1 Very low
Scoring algorithm for IIEF
All items are scored in five domains as follows:

Domain	**Items**	**Range**	**Score max Score**
Erectile function	1, 2, 3, 4, 5, 15	0–5	30
Orgasmic function	9, 10	0–5	10

(continued)

Table 12.3 (continued)

Domain	Items	Range	Score max Score
Sexual desire	11, 12	0–5	10
Intercourse satisfaction	6, 7, 8	0–5	15
Overall satisfaction	13, 14	0–5	10

adjunctive sexual function measure for the sildenafil clinical trials [159] and has since gained universal acceptance as the leading instrument to assess male erectile function. A 5 question –shorter form (SHIM-5) was subsequently developed, which has been utilized quite widely as well [160] (Table 12.4). The IIEF and its shorter version, the SHIM-5, have been used for all the clinical phosphodiesterase type 5 inhibitor trials along with numerous non-pharma-sponsored trials. The IIEF contains 15 questions which ask the patient to recall sexual activity for the previous 4 weeks. The 15 questions are answered on a Likert- type scale which allows the instrument to be graded numerically. Questions 1–5 and 15 are termed the erectile function domain of the IIEF. An IIEF total score of 26–30 indicates normal erectile function, and a score of 10 or less indicates severe ED.

Male ejaculatory function may be assessed by a variety of instruments. A recent, noteworthy instrument is the Male Sexual Health Questionnaire, which has been shortened to a 4 –question instrument [161] (Table 12.5).

Testosterone deficiency in the male can be assessed by a variety of instruments. The Androgen Deficiency in the Aging Male (ADAM) questionnaire is widely used but unfortunately is not validated [135]. Further, the ADAM questionnaire (Table 12.6) seems to be sensitive but not specific for the diagnosis of hypogonadism. An answer of YES to questions 1 or 7 or any 3 other questions, suggest that the patient may be experiencing androgen deficiency (low testosterone level). The Aging Males' Symptom (AMS) questionnaire is often utilized as well [32]. Recently, the NERI hypogonadism screener has been published, but has not yet found its way into routine clinical practice [162].

The Centers for Epidemiologic Study –Depression scale is a public domain, user-friendly instrument to assess depressive symptoms [200]. It is easily interpreted and its use is encouraged.

Female Sexual Function Assessments

There are several well-designed, validated, instruments that assess female sexual function [129]. One such instrument that seems to be gaining in popularity is the Female Sexual Function Index (FSFI). The FSFI is a brief multidimensional scale for assessing sexual function in women. The scale has received psychometric evaluation, including studies of reliability, convergent validity, and discriminant validity. The authors' found an FSFI total score of 26.55 to be the optimal cut score for differentiating women with and without sexual dysfunction [202]. The FSFI has been recently validated for use in cancer survivors [13].

Table 12.4 The International Index of Erectile Function (IIEF-5) questionnaire

5-item version of the International Index of Erectile Function (IIEF-5) as a diagnostic tool for erectile dysfunction.					
Over the past 6 months:					
1. How do you rate your **confidence** that you could get and keep an erection?	Very low 1	Low 2	Moderate 3	High 4	Very high 5
2. When you had erections with sexual stimulation, **how often** were your erections hard enough for penetration?	Almost never/never 1	A few times (much less than half the time) 2	Sometimes (about half the time) 3	Most times (much more than half the time) 4	Almost always/ always 5
3. During sexual intercourse, **how often** were you able to maintain your erection after you had penetrated (entered) your partner?	Almost never/never 1	A few times (much less than half the time) 2	Sometimes (about half the time) 3	Most times (much more than half the time) 4	Almost always/ always 5
4. During sexual intercourse, **how difficult** was it to maintain your erection to completion of intercourse?	Extremely difficult 1	Very difficult 2	Difficult 3	Slightly difficult 4	Not difficult 5
5. When you attempted sexual intercourse, **how often** was it satisfactory for you?	Almost never/never 1	A few times (much less than half the time) 2	Sometimes (about half the time) 3	Most times (much more than half the time) 4	Almost always/ always 5
IIEF-5 scoring: The IIEF-5 score is the sum of the ordinal responses to the five items. 22–25: No erectile dysfunction 17–21: Mild erectile dysfunction 12–16: Mild to moderate erectile dysfunction 8–11: Moderate erectile dysfunction 5–7: Severe erectile dysfunction					

Reproduced with permission from Rosen et al. [160]

Table 12.5 EjD short form for assessing EjD* 5 or less on the SD domain of the FSFI as having HSDD and those with SD scores of 6 or more as not having HSDD maximized diagnostic sensitivity and specificity

In the past month:
1. How often have you been able to ejaculate or "cum" when having sexual activity?
5 – All the time
4 – Most of the time
3 – About half the time
2 – Less than half the time
1 – None of the time/could not ejaculate
2. How would you rate the strength or force of your ejaculation?
5 – As strong as it always was
4 – A little less strong than it used to be
3 – Somewhat less strong than it used to be
2 – Much less strong than it used to be
1 – Very much less strong than it used to be
0 – Could not ejaculate
3. How would you rate the amount or volume of semen or fluid when you ejaculate?
5 – As much as it always was
4 – A little less than it used to be
3 – Somewhat less than it used to be
2 – Much less than it used to be
1 – Very much less than it used to be
0 – Could not ejaculate
4. If you have had any ejaculation difficulties or have been unable to ejaculate, have you been bothered by this?
0 – No problem with ejaculation
1 – Not at all bothered
2 – A little bothered
3 – Moderately bothered
4 – Very bothered
5 – Extremely bothered

Reproduced with permission from Rosen et al. [161]
In the development sample, the sensitivity and specificity for predicting HSDD (with or without other conditions) were 75 % and 84 %, respectively, and the corresponding sensitivity and specificity in the validation sample were 92 % and 89 %, respectively MSHQ

While this validated cutpoint for the total Female Sexual Function Index scale score of 26.55 enables one to classify women into groups with and without sexual dysfunction, there was no sexual desire (SD) domain-specific cut-off point for assessing the presence of diminished desire in women with or without a sexual desire problem. Gersterberger et al. developed the optimal cut-off point for diagnosis of HSDD on the SD domain of the FSFI: SD scores of 5 or less were considered to have HSDD and SD scores of 6 or more did not. In the development sample, the sensitivity and specificity for predicting HSDD (with or

Table 12.6 Center for Epidemiologic Studies Depression Scale (CES-D), NIMH

Questions used as part of the Saint Louis University ADAM questionnaire
1. Do you have a decrease in libido (sex drive)?
2. Do you have a lack of energy?
3. Do you have a decrease in strength and/or endurance?
4. Have you lost height?
5. Have you noticed a decreased "enjoyment of life"?
6. Are you sad and/or grumpy?
7. Are your erections less strong?
8. Have you noted a recent deterioration in your ability to play sports?
9. Are you falling asleep after dinner?
10. Has there been a recent deterioration in your work performance?

Table reproduced with permission from Morley et al. [135]

without other conditions) were 75 % and 84 %, respectively, and the corresponding sensitivity and specificity in the validation sample were 92 % and 89 %, respectively [61].

Another tool used to assess female sexual dysfunction is the Female Sexual Distress Scale (FSDS) and the Female Sexual Distress Scale-Revised (FSDS-R) [36, 37]. The FSDS is a 12 question survey that relates to different aspects of sexual distress. The FSDS-R is the FSDS with an additional question about how bothered the patients are about their low sexual desire [37]. In determining HSDD vs. no sexual dysfunction during the original validation study, the sensitivity of the FSDS was 86 %, specificity 93 %, and PPV 0.9 at the optimal cutoff of ≥15 points [36]. In the validation study of the FSDS-R, the optimal cutoff was ≥11. The cutoff produced a sensitivity of 92.7 %, specificity of 96 %, and PPV 0.93 for patients with HSDD vs. no FSD during day 0 survey results [37]. The retest reliability and internal consistency of both scales were also tested and proven. The survey scores for HSDD vs. another FSD were similar and the survey could not accurately differentiate them.

It is important to recognize that many clinicians find these questionnaires somewhat cumbersome to use during the office visit. Rather than using the full instrument, clinicians have adopted their practices so that they utilize a modified version of a specific instrument. This seems to suit them well.

There are many other wonderful instruments that have been developed to assess male and female sexual function. The authors of these fine instruments deserve recognition and we offer our apologies due to our inability to include them and credit them in this section. Finally, there are many instruments that evaluate mood, depression, cognition, strength, quality of life, amongst other areas, in the aging male and female. Discussions of these instruments are beyond the scope of this chapter.

Cardiovascular evaluation of the male and female patient with sexual dysfunction: Consensus guidelines have provided algorithms to the clinician as to which

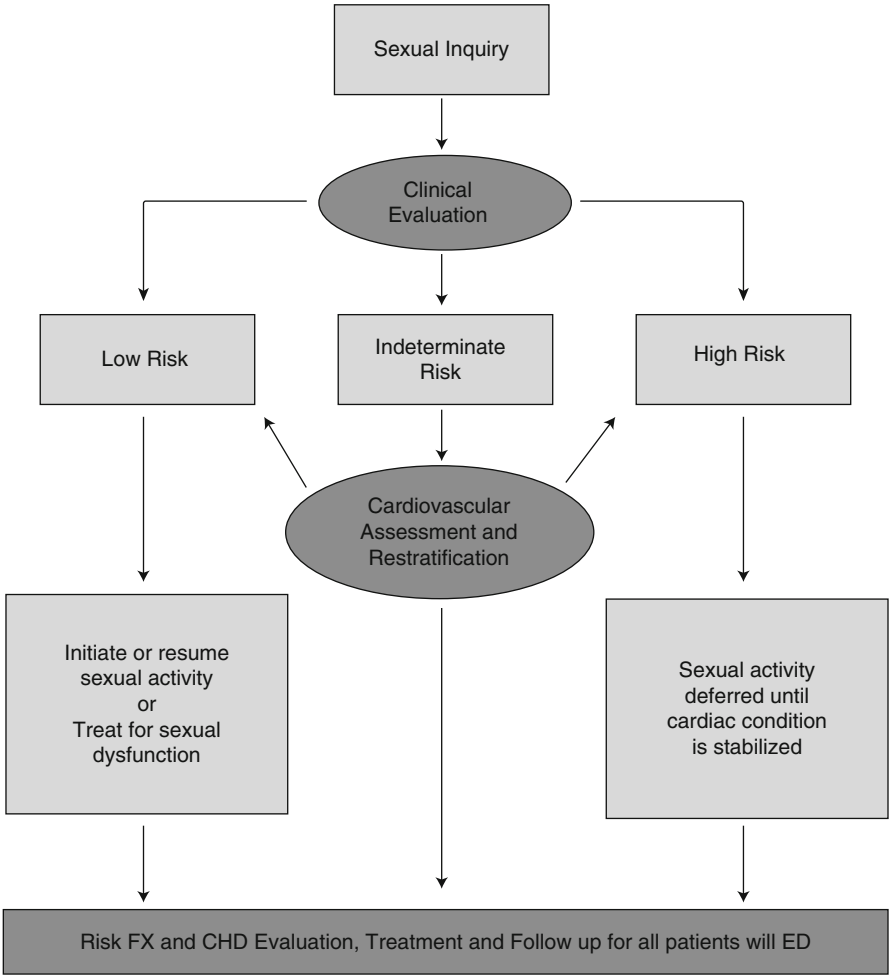
Sexual Inquiry
Clinical Evaluation
Low Risk
Indeterminate Risk
High Risk
Cardiovascular Assessment and Restratification
Initiate or resume sexual activity or Treat for sexual dysfunction
Sexual activity deferred until cardiac condition is stabilized
Risk FX and CHD Evaluation, Treatment and Follow up for all patients will ED

Fig. 12.1 Risk assessment algorithm for men with cardiovascular risk factors who wish to reengage in sexual activity (Reproduced with permission from Kostis et al. [98])

patients with cardiovascular risk factors may safely re-engage in sexual activity. The Princeton II and III consensus guidelines document discusses the approach for men with a variety of CV risk factors and their ability to re-engage in sexual activity [98, 143] (Fig. 12.1). Low risk patients are those with less than 3 CV risk factors, controlled hypertension, etc. We recommend that readers review [98, 143] to gain a better understanding of the risk assessment algorithm. Importantly, data from the Princeton III conference has surfaced that reviews CV risk and female sexual health [131]. Other, recent guidelines have been offered to assist the clinician with counseling patients who have various CV issues and wish to reengage in sexual activity [111].

Sexual Dysfunction in Women

Sexual dysfunction in women is somewhat difficult to study because symptoms and diagnosis are subjective and variable depending on study. Most of what we currently know come from collections of voluntary surveys and it is difficult to assess for bias within these answers or the clinical significance of any change in survey answers. The response rate in these surveys is highly variable from 9 % [104] to 82 % [189], and possibly subject to selection bias. To further complicate matters, there is a large number of psychological, social, medical, and surgical problems are known to cause sexual dysfunction [90]. In this study, we will not attempt to cover all those causes; we will cover the etiologies and treatments that are most relevant to an aging woman. The most relevant of which is menopause, which leads to a series of hormonal changes and physical changes to the vulva, vagina, and lower urinary tracts. Other relevant factors include the availability of a partner and decline in general health.

Prevalence of Sexual Dysfunction in Elderly Women

According to major surveys [103, 104, 116, 144, 189], the percent of sexually active elderly female who experienced any sort of sexual problem was 39–58 %. The most common sexual dysfunctions were (1) low desire, (2) lubrication problems, and (3) inability to climax.

The Global Study of Sexual Attitudes and Behaviors multinational study [103] collected data from 27,500 men and women aged 40 to 80 years of age using standardized questionnaires. For women, the lack of sexual desire (21 %), inadequate lubrication (16 %), and the inability to reach organism (16 %) were the most common sexual problems. There are limited quantitative or qualitative criteria for diagnosis of female sexual dysfunction. A survey of a probability sample of 3005 U.S. adults age 57–85, found that about 50 % of females reported at least 1 bothersome sexual problem [116]. Low desire (43 %), difficulty with lubrication (39 %), and inability to climax (34 %) were the most common problems. In a study of American adults age 40–80 via telephone interview, found that the most common sexual problems were lack of interest (33.2 %), lubrication difficulties (21.5 %), and inability to reach orgasm (20.7 %) [102].

Of note, the rate of sexual dysfunction in elderly females is not strikingly higher than sexual dysfunction in younger women. Laumann et al. [101] analyzed data from the National Health and Social Life Survey, a probability sample study of sexual behavior in a demographically representative, cohort of US adults. A national probability sample of 1749 women and 1410 men aged 18–59 years at the time of the survey, demonstrated that 43 % of women surveyed had sexual dysfunction; 22 % had a low sexual desire category; 14 % had arousal problems, and 7 % had sexual pain. Comparing this study with studies of elderly population shows that

while more elderly people have sexual dysfunction many of these dysfunctions were present at a prior stage of the patient's life. The major exception to this rule would be problems with lubrication, which is not prevalent in this study of younger women.

It is important to note that while sexual rate of certain types of sexual dysfunction increases with age, they aren't necessarily problematic. Low sexual desire does not become hypoactive sexual desire disorder if the patient is not distressed by the problem. A cross-sectional survey characterizing low sexual desire and HSDD in relation to menopause [199], found that even though low sexual desire was found in 39.7 % and 52.7 % of women with surgical and natural menopause respectively, only 12.5 % and 6.6 % of those patients met the criteria for HSDD. The Rancho Bernardo study is a survey of 1303 mostly upper class women age over 40 (average: 67) on general health, recent sexual activity, sexual satisfaction, and the Female Sexual Function Index questionnaire (FSFI). Approximately half (49.8 %) reported sexual activity within the past month with or without a partner, the majority of whom reported arousal (64.5 %), lubrication (69 %), and orgasm (67.1 %) at least most of the time. Approximately third reported low, very low, or no sexual desire. Although frequency of arousal, lubrication, and orgasm decreased with age, the youngest (≤55 years) and oldest (≥80 years) group reported a higher frequency of orgasm satisfaction. Emotional closeness during sex was associated with more frequent arousal, lubrication, and orgasm; estrogen therapy was not. Overall, two thirds of sexually active women were moderately or very satisfied with their sex life, as were almost half of sexually inactive women [189].

Hormonal Issues in the Female: Menopause

Menopause is defined as the permanent cessation of menses occurring usually between the ages of 45 and 55 with estrogen deficiency as the primary diagnostic criterion [92, 204]. The symptoms include hot flashes, sexual dysfunction, mood disorders, and urogenital symptoms and it increases the risk for cardiovascular, musculoskeletal, and psychogenic sequelae. Diagnosis is usually made in women with follicle stimulating hormone (FSH) levels greater than 40, although FSH is not the most accurate way to assess menopausal status as FSH levels may vary considerably from the transition to pre- and peri-menopause to menopause [204]. In menopause occurs before the age of 40, it is considered pathologic and a workup should be initiated. This is considered premature ovarian failure and is usually secondary to autoimmune oophoritis [204]. Bilateral oophorectomy can also induce menopause.

Although the changes brought on by menopause are, for the most part, considered adverse, some women feel relaxed and liberated from the fear of pregnancy. Others experience a psychologic decrease of what they consider as their sexuality and femininity. The vaginal changes associated with menopause can cause dyspareunia and worsen the sexual experience. Lower estrogen levels also predispose menopausal women to atrophic vaginitis and more frequent vaginal infections which are associated with itching, burning, and discharge [92, 204].

Several recent studies sought to estimate the effect of menopausal status on low sexual desire and hypoactive sexual desire disorder (HSDD) in US women. West et al. [199] performed a cross-sectional phone interview of 2207 US women aged 30–70 years and in stable relationships (≥3 months). The analysis focused on 755 premenopausal women and 552 naturally and 637 surgically menopausal women. The prevalence of low sexual desire ranged from 26.7 % among premenopausal women to 52.4 % among naturally menopausal women. The overall rate of HSDD was 8.3 %. The prevalence of HSDD was highest among surgically menopausal women (12.5 %) and lowest in natural menopausal women (6.6 %). Compared with premenopausal women, the adjusted prevalence ratios for HSDD were 2.3 (95 % confidence interval, 1.2–4.5) for surgically menopausal women and 1.2 (0.5–2.8) for naturally menopausal women; the prevalence ratios for low sexual desire were 1.3 (0.9–1.9) and 1.5 (1.0–2.2) for surgically and naturally menopausal women, respectively. Leiblum et al. [107] analyzed the Women's International Study of Health and Sexuality questionnaire of U.S. women and looked at HSDD in pre-menopause, surgical menopause, and natural menopause patients. Leiblum et al. showed that in HSDD was greatest amongst surgical post-menopausal women age 20–49 (26 %), compared to 14 % in pre-menopausal women of the same age. They also showed no difference in HSDD between surgical and natural menopause women age 50–70.

There are also studies suggesting that surgical menopause have no effects on HSDD. Both Aziz et al. [8] and Teplin et al. [183] observed the well-being of patients that elected for TAH-BSO vs. TAH only for benign indications. Both found no differences between the groups in terms of differences of sexual satisfaction and well-being for 1–2 years after the surgery. Graziottin et al. [68] surveyed patients with surgical menopause in 4 different European countries and found that low sexual desire was similar between the countries but HSDD rates were different, suggesting the role of culture and HSDD. In summary, while low desire is more prevalent in post-menopausal women, there is no evidence that natural menopause is associated with HSDD. With regards to surgical menopause, there is weak evidence that surgically menopausal women results in a higher rate of HSDD, likely due to the more unexpected nature of the change.

Treat of Female Sexual Dysfunction

There are currently numerous treatment options for treatment of sexual dysfunction associated with aging and menopause.

Estrogen Replacement Therapy

For decades estrogen replacement therapy (ERT) had been the mainstay of treatment for menopausal women for decades under the premise that it safeguards against osteoporosis and cardiovascular disease. Data from the Women's Health Initiative

E-Alone Trial revealed that ERT may result in increased cardiac events and cerebrovascular disease in healthy women as well as an increased risk of venous thromboembolism [157]. There was also concern regarding ERT predisposing women to higher risks for breast and uterine cancers [18]. Thus, the use of ERT fell out of favor. The current focus is on treating the sequelae of symptoms such as osteoporosis, postmenopausal depression, and sexual dysfunctions, without the use of ERT.

Topical Non-hormonal Therapy

There are a number of over-the-counter lubricants available to treat vaginal dryness and the dyspareunia associated with them. According the North American Menopause Society [145], this is the 1st line of treatment for vulvovaginal symptoms. While this treatment is harmless and alleviates some symptoms, it does not reverse the underlying changes that cause these symptoms and do not typically work for more severe symptoms [95].

Topical Hormonal Therapy

Topical estrogen therapies come in the form of a tablet, ring, or ointment. Local estrogen allows for reversal of the physiology associated with menopause without the cardiovascular and oncologic side effects of systemic estrogen. Studies have shown that topical estrogen can decrease vaginal pH, increase lactobacilli colonization, and shift the cell-balance to represent that of a pre-menopausal state [145]. Additionally, in a meta-analysis of randomized control trials comparing topical estrogen to other treatments modalities it was found to be equally effective compared to systemic estrogen in treating vaginal symptoms and superior to non-hormonal moisturizers when there was 2 or more symptoms present [150] Risk of endometrial cancer in these studies was exceedingly low rate; among 600 patients in 6 studies that took endometrial biopsies, only 1 case of endometrial cancer was found. However, it should be noted that all studies lasted 1 year or less, so long-term use and side effects of local estrogen is unknown.

Testosterone Therapy

Testosterone is a major drive in female sexual desire, arousal, as well as multiple other anabolic processes such as bone mineral content and muscle building [10]. Testosterone is secreted by the ovaries and drops by as much as 50 % during menopause and can lead to a constellation of symptoms including decreased sexual

function [100]. In a meta-analysis of 35 RCTs, Elraiyah et al. [46] studied the addition of testosterone therapy to treat menopausal symptoms in females with normal adrenal function. They found that the addition of testosterone (either used alone or with ERT) use improves various markers of sexual outcomes psychological well-being, most noticeably number of satisfying sexual episodes in 28 days (SMD = 1.2, $p < 0.001$). The major side effects of testosterone were a change in lipid profile of unknown cardiovascular significance. There was a small increase in LDL cholesterol (2.62 mg/dL; $p < 0.03$), decrease in HDL (12.89 mg/dL; $p < 0.01$), decrease in TG (−15.29 mg/dL; $p < 0.001$), and total cholesterol (−8.51 mg/dL; $p = 0.001$). Patients also had a small increase in risk of acne (RR = 1.62; $p < 0.001$) and hirsutism (RR =1.45; $p = 0.011$). There were no significant risks or benefits in bone health or body weight. Davis and Braunstein [33] performed a similar meta-analysis and showed that testosterone was effective in treating HSDD in post-menopausal women in terms of various measurements of sexual desire and satisfaction (SSE increased 2.1 vs. 0.7 placebo; $p < 0.001$). The major limitation to the use of testosterone is that long-term evidence is extremely limited; most of the studies included in the meta-analysis by Elraiyah et al. [46] lasted less than 1 year (median follow-up was 6 months). In addition, many of those studies looked at the use of testosterone in conjunction with ERT, which is no longer a popular option for sexual dysfunction. Last, with most other literature in female sexual dysfunction, the only way to measure outcome is via voluntary surveys subject to response bias and selection bias.

A similar meta-analysis looked at various forms of DHEA as possible treatment for female sexual dysfunction [45]. The study incorporated 1188 patients across 23 RCTs comparing DHEA and placebo and found that DHEA did not significantly improve sexual function in post-menopausal women. DHEA did not have any adverse effects in terms of lipid profile, glucose, body weight, and bone density though only 2 of these studies lasted more than a year.

SERM Therapy

Since the precipitous decline in the use of estrogen therapy after the Women's Health Initiative trials, there has been a demand for hormonal therapy for menopausal symptoms and menopause-associated sexual dysfunction that do not have the cardiovascular and oncologic side effects of estrogen. In 2013, Ospemifene (Osphena) 60 mg daily became the first selective estrogen receptor modulator (SERM) to be FDA-approved for sexual dysfunction associated with post-menopausal vulvovaginal atrophy [52]. During menopausal transition, several changes occur to the vulvar and vaginal epithelium, including increase in pH, decreased thickness of epithelium layer, decrease in superficial and intermediate cells, and increase in parabasal cells. These changes lead to a constellation of symptoms including UTIs, yeast infections, vaginal dryness, dyspareunia, and itching. Ospemifene exerts a strong estrogenic effect on the vaginal epithelium to reverses these physiologic trends and improve symptoms [194].

Ospemifene has gone through all three phases of clinical trials and has shown to improve the underlying physiology as well as the vulvovaginal symptoms associated with menopausal changes. In a meta-analysis of the 6 phase 3 RCTs involving 1772 patients, Ospemifene is not only safe, but capable of reversing both the physiological changes as well as the symptoms of menopause [29]. A 12-week course of involving 1228 patients in 3 of the RCTs showed that Ospemifene was able to induce significant increase in superficial cells (+9.24 %, $p<0.00001$), and decrease in vaginal pH (−0.89, $p<0.00001$), decrease in parabasal cells (−37.5 %, $p<0.00001$). The meta-analysis also reported improvements in dyspareunia severity score (−0.37, $p<0.00001$) and greater endometrial thickness (0.51 mm, $p<0.00001$) compare to placebo.

Evidence of long-term safety currently includes 3 RCTs comparing Ospemifene to placebo over a 52 week period. The most common side effects were hot flashes, vaginal discharge, and muscle spasms, though they were rarely serious enough to lead to discontinuation [65, 177]. In terms of endometrial safety, while Ospemifene slightly increase endometrial thickness [207], there have been no evidence of increased risk to endometrial hyperplasia. Of the 2 RCTs studying patients with an intact uterus [65, 177], 1 in 500 patients who were biopsied at the end of the 52-week trial developed endometrial hyperplasia and no patients developed endometrial cancer. None of the 52-weeks phase III RCTs reported development of breast cancer in Ospemifene-treated patients. The risk of cardiovascular events (i.e., stroke, MI, DVT) was similar between patients treated with Ospemifene vs. placebo, rare, usually unrelated to treatment [65, 177, 207]. None of the studies reported changes in lipids, coagulation, and hematologic lab results. These studies demonstrate that Osfemipene use provides sexual and vulvovaginal benefits and no evidence of harmful effects on the cardiovascular system, breast, and endometrium. However, it should be noted that these patients were followed for only 1 year and the long-term effects of Ospemifene beyond 1 year is not known.

Others SERMS (i.e., Raloxifene) have been tested and found ineffective at treating vulvovaginal symptoms associated with menopause.

Flibanserin – First FDA Approved Drug for Hyposexual Desire Disorder

Flibanserin is a post-synaptic agonist of serotonin receptor 1A and antagonist of serotonin receptor 2A. Initially developed as an anti-depressant, Flibanserin was found to increase sexual desire in females and received further evaluation as a treatment for HSDD [93]. The exact mechanism is believed to involve modulation of neurotransmitters such as dopamine, serotonin, and norepinephrine in the CNS [176].

On August 18th, 2015, the FDA approved, Flibanserin 100 mg QHS as the first ever medication to treat pre-menopausal females with acquire, generalized hypoactive desire sexual disorder [51]. This came after extensive controversy and two previous rejections in 2010 and 2013.

The evidence for Flibanserin in pre-menopausal women revolves around 3 blinded placebo-controlled RCT's: The BEGONIA, DAISY, and VIOLET trials. The BEGONIA trial compared pre-menopausal women to flibanserin 100 mg QHS (n = 545) or placebo (n = 545) for 24 weeks with Satisfying Sexual Events (SSE) over 28 days and FSFI-desire domain score as the primary end-point [88]. The VIOLET trial compared pre-menopausal women to flibanserin 100 mg QHS (n = 290), flibanserin 50 mg QHS (n = 295), or placebo (n = 292) for 24 weeks with sexually satisfying experience (SSE) over 28 days and sexual desire score measured daily using an electronic diary (eDiary) as the primary end-point [38]. The DAISY trial compared pre-menopausal women to flibanserin mg 25 BID (n =396), flibanserin 50 mg BID (n = 392), flibanserin 100 mg QHS (n = 395) or placebo (n = 398) for 24 weeks with SSE over 28 days and daily e-diary sexual desire score as the primary end-point [186]. FSFI-total score, FSFI desire domain, FSDS-R, FSDS-R item 13, and PGI-I were also used evaluated as secondary end points. All of these RCTs show that flibanserin 100 mg QHS yielded maximal benefits. A meta-analysis of these 3 studies yielded a benefit of 100 mg QHS compared to placebo for the following parameters: SSE (SMD = 0.88, $p < 0.00001$), daily sexual desire score (SMD = 1.91, $p = 0.03$), FSFI desire domain score (SMD = 0.33, $p < 0.0001$), FSFI total score (SMD = 1.86, $p < 0.00001$), FSDS-R total score (SMD = −3.14, $p < 0.00001$), and PGI-G score (SMD = 1.95, $p < 0.00001$). The OR of all adverse events was 1.54, most of which were mild or moderate severity. The most common side effects were dizziness (9.0–12.1 %), nausea (7.6–11.9 %), somnolence (11.0–14.4 %), headaches (7.6–11.4 %) and fatigue (5.7–9.6 %). Adverse events leading to discontinuation and severe/serious adverse events were higher in the treatment arm for all 3 trials. The SUNFLOWER trial, a 12-month open label study [80], exhibited a 9.5 % chance having serious or severe side effects and 10.7 % women with AE leading to discontinuation. In summary, flibanserin provides modest benefits in several assessments of sexual desire, sexual distress, and overall sexual well-being. However, the benefits should be weighed against an increased risk of adverse events, some of which may be severe and lead to discontinuation of medication.

There is one double-blinded RCT looking at flibanserin in comparing flibanserin 100 mg QHS vs placebo in naturally post-menopausal women for 24 weeks. The benefits of flibanserin were less pronounced and the risk profile was similar [176]. For example, the SSE SMD was 0.4 compared to 0.9 in pre-menopausal studies. The FDA has yet to approve flibanserin for post-menopausal women.

It should be noted that the outcome measures used by the FDA for the female sexual dysfunction drug development process remain a significant challenge in the field of female sexual dysfunction. Assessing the sexual response in women with female sexual dysfunctions (FSDs) in clinical trials remains difficult. Part of the challenge is the development of meaningful and valid end points that capture the complexity of women's sexual response. The authors wished to highlight the shortcomings of daily diaries and the limitations of SSEs as

primary end points in clinical trials of women with HSDD as recommended by the FDA in their draft guidance on standards for clinical trials in women with FSD. Nine placebo-controlled randomized trials in women with HSDD were reviewed: seven with transdermal testosterone and two with flibanserin. In four trials, all using transdermal testosterone 300 μg/day had agreement between changes in SSEs, desire, and distress. In five studies (testosterone 300 μg/day, n = 2; testosterone 150 μg/day, n = 1; flibanserin n = 2), changes in SSEs did not correlate with changes in desire and/or distress and vice versa. It should be noted that in the flibanserin trials, SSEs did correlate with desire assessed using the Female Sexual Function Index but not when it was assessed using the daily eDiary. Hence, the findings in the literature do not uniformly support the recommendations from the FDA draft guidance to use diary measures in clinical trials of HSDD as primary end points. Patient-reported outcomes appear to be better suited to capture the multidimensional and more subjective information collected in trials of FSD [96]. Future research will hopefully answer these important study endpoint questions and other important research questions.

Treatment of Urinary Incontinence and Sexual Dysfunction

There are a group of women who have urinary incontinence and sexual dysfunction. Surgical or medical correction of the incontinence may improve the sexual issues [56, 113]. This is an underappreciated area of medical need for older women interested in restoration of sexual function.

As an example, one hundred fifty-seven women complaining of urodynamic stress incontinence underwent a mid-urethral sling (MUS) procedure [56]. All patients answered the Italian translation of FSFI, before and 12 months after surgery. Also included in the final analysis were all the women who are nonsexually active at baseline were also included. The authors evaluated the prevalence of female sexual dysfunction according to the FSFI cutoff point of 26.55.

One hundred thirty-three patients completed the study protocol: 105 out of 133 underwent to a trans-obturator procedure, while 28 out of 133 had a retropubic procedure. After the 12-month follow up, 115 out of 133 patients (86 %) were dry, 10 improved their symptoms, and the remaining 8 were unchanged. Seventy-nine out of 133 (59 %) patients reported an active sexual life before surgery. Fifty-four (41 %) reported they were not sexually active before surgery. Twelve months after surgery, 22 out of 54 nonsexually active women (40 %) reestablished sexual activity, whereas only 6 out of 79 (7.5 %) patients, sexually active at baseline, were not sexually active 1 year after surgery ($P < 0.05$). After adjusting for multiple testing, only age, menopause, and storage symptoms remained significantly correlated with the FSFI total score post-surgery as independent variables. These data showed that after a MUS procedure, female sexual function improves and a very relevant percentage of non-sexually active women reported renewed sexual activity after MUS.

Sexual Dysfunction in Men

Sexual dysfunction in men can occur in any one of the four stages of sexual response cycle: excitement, plateau, orgasm/ejaculation, and resolution. For men, the most common sexual dysfunction in the young and old are erectile dysfunction and ejaculatory/orgasmic dysfunction. In a large survey study of adults age 57–85, erectile difficulties was the most prevalent problem (37 %) and increases to 44 % in patient groups 65–74 and 75–85 [116]. A large, multinational study collected data from 27,500 men and women aged 40–80 years of age using standardized questionnaires found that the most common dysfunctions for men were early ejaculation (14 %) and erectile dysfunction (10 %); ejaculatory disorders being more common in men age 40–49, 50–59, and 60–69 and erectile difficulties being most ages 70–80 [144]. Other common sexual problems in the geriatric population include low desire, and performance anxiety.

Erectile Dysfunction

Erectile dysfunction is defined as the inability to achieve or maintain an erection sufficient for sexual activity. Approximately 152 million men worldwide and as many as 30 million American men are affected by erectile dysfunction. As many as 322 million men worldwide are projected to have erectile dysfunction by 2025 [82, 125]. 18 million American men 40–70 years of age are estimated to be affected with some degree of erectile dysfunction [82, 125]. It has also been demonstrated that prevalence of erectile dysfunction increases significantly with age [54, 76, 101, 125, 144]. Based on the Massachusetts Male Aging Study, a large epidemiologic study, the crude incidence rate of erectile dysfunction was 25.9 cases per 1000 man-years [54]. The annual incidence rate increases with age from 12.4 cases per 1000 men years in American men ages 40–49 years to 46.5 cases per 1000 men-years for men 60–69 years of age [54] (Fig. 12.2). In another study, erectile dysfunction increases from 5 % in men age 40–49 to 22 % in men age 70–80.

Causes of Erectile Dysfunction

There are countless etiologies of erectile dysfunction. In general, they can be categorized into several categories: psychogenic, neurogenic, endocrine, vascular, iatrogenic, and mixed (Table 12.7).

ED can be caused by endocrine abnormalities, most commonly DM, but also hypogonadism, hypothyroidism, and hyperprolactinemia [130, 167, 169, 170]. DM alters in neurotransmitters like nitric oxide, vasoactive intestinal peptide, and pro-inflammatory hormones such as TNF-α and IL10, thus resulting in poor erectile

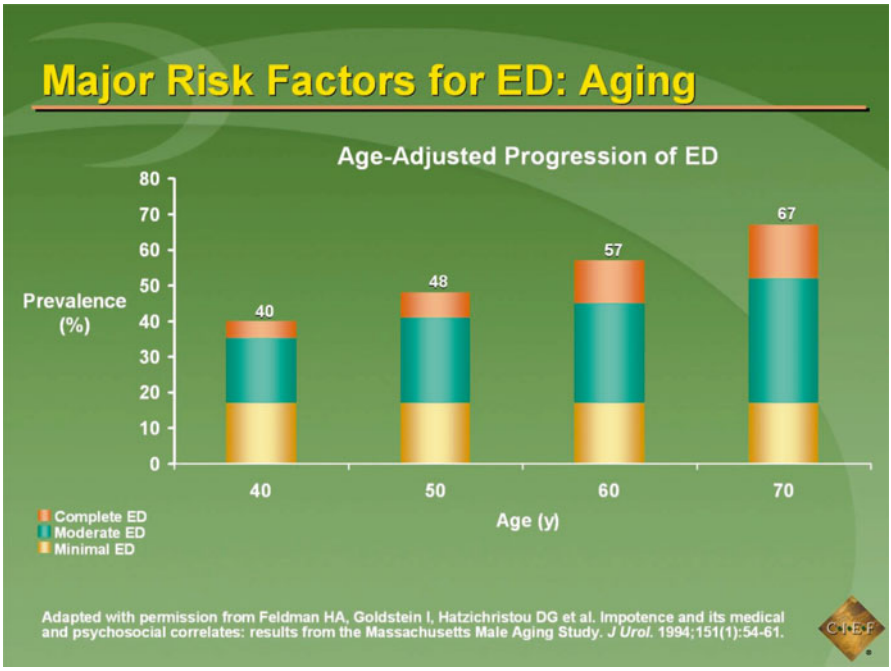

Fig. 12.2 The landmark Massachusetts Male Aging Study (MMAS), a community-based observational study of nearly 3000 men, aged 40–70 years, clearly established that ED is highly prevalent, age related, and progressive. Subjects (n = 1290) were asked to respond to a sexual activity questionnaire characterizing their level of ED. *Minimal* ED was defined as "usually able to get or keep an erection"; *moderate*, as "sometimes able"; and *complete*, as "never able to get and keep an erection." Self-rated ED was reflected by higher frequency of erectile difficulty during intercourse, lower monthly rates of sexual activity and erection, and lower satisfaction with sex life and partner (Adapted with permission from Feldman et al. [54])

ability [34, 119, 151] See Fig. 12.3 for illustration of these interactions [71]. Complications of smooth muscle and endothelial dysfunction are sequelae of DM, which can exacerbate the severity of ED by direct pathophysiology. In patients with diabetic neuropathy, diabetes may also affect erectile function by weakening the afferent and efferent neurologic signaling pathways essential for sexual function [15, 106].

Vascular and hypertensive disease can worsen the severity of ED and bring an earlier onset of impotence. The primary mechanisms are arterial insufficiency and venous leakage. Atherosclerosis leads to arterial occlusive disease, which can decrease the perfusion pressure and arterial flow to the lacunar spaces necessary for penile rigidity [119]. Subsequently, adequate pressure is not achieved within the corpora cavernosa because of excessive venous outflow through the subtunical venules and thus no erection occurs [73, 74].

Other causes include neurologic deficits such as cerebrovascular accidents (CVA), Parkinson's disease, multiple sclerosis, and spinal cord injury. Direct injury to the penis itself either by trauma or by other pathologies like priapism can contrib-

Table 12.7 Classification of erectile dysfunction

Category	Common etiologies	Pathophysiology
Psychogenic	Performance anxiety Psychologic stress Psychiatric disorders	Central inhibition Decreased libido
Neurogenic	Stroke Pelvic surgery CNS disorders (i.e., Multiple Sclerosis) Trauma Spinal cord injury	Inadequate neural transmission
Hormonal	Hypogonadism Chemotherapy Chronic disease Hyperprolactinemia	Central inhibition Inadequate NO release
Vascular	Trauma Diabetes Hypertension Atherosclerosis	Inadequate arterial flow Poor venous obstruction
Drug-induced	β-Blockers Androgen deprivation therapy Smoking Anti-depressants Anti-psychotics	Central inhibition Vascular or neural compromise

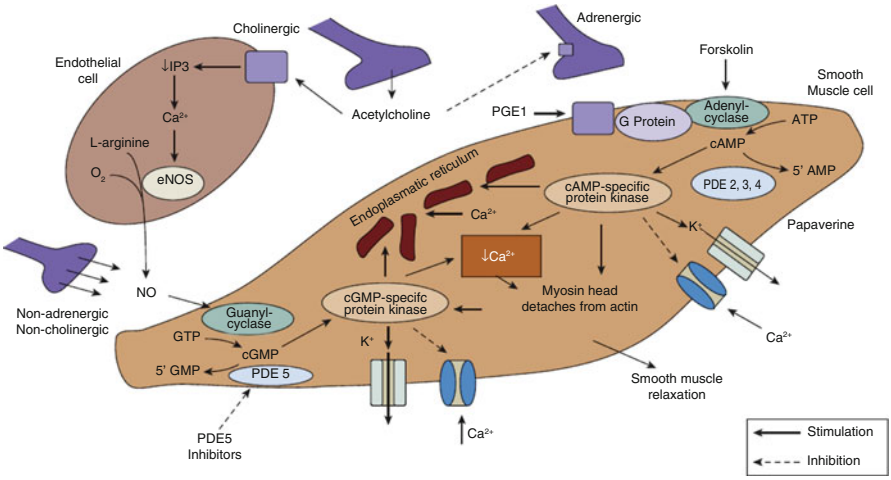

Fig. 12.3 Regulation of penile corpus cavernosum smooth muscle relaxation and effect of PDE5 inhibitors. *ATP* adenosine triphosphate, *cAMP* cyclic adenosine monophosphate, *cGMP* cyclic guanosine monophosphate, *eNOS* endothelial nitric oxide synthase, *GTP* guanosine-50-triphosphate, *IP3* inositol trisphosphate, *NO* nitric oxide, *PDE* phosphodiesterase, *PGE1* prostaglandin E1 (Reproduced with permission from Hatzimouratidis et al. [71])

ute to varying degrees of ED. Finally there are several psychogenic causes such as anxiety, depression, and stress-related issues that decrease the strength and duration of an erection or outright prevent initiation of the erection.

Although the clinical presentation of ED is the same, the diagnosis requires a complete history and physical to look for the etiology. Physical exam should especially look for Peyronie's plaque, secondary sexual characteristics, blood pressure assessment, and evidence of vascular disease. Laboratory values of blood glucose, cholesterol, and testosterone levels usually supplement an evaluation [170].

In this section, our focus is on the most common and profound causes of ED in the elderly population and approaches that addresses the problem as a whole.

Erectile Dysfunction and Metabolic Syndrome

There is a well-established link between metabolic syndrome and erectile dysfunction. The definition of metabolic syndrome varies depending on the study, but they all emphasize several key ingredients: obesity, hypertension, hyperlipidemia, and diabetes mellitus. Lifestyle factors that contribute to metabolic syndrome, such as smoking, lack of exercise, and diet, were also evaluated. The triad of hypertension, hyperlipidemia, and diabetes mellitus alters the physiology of erections in multiple ways (as mentioned above). Clinically, strong evidence linking metabolic syndrome to erectile dysfunction and growing evidence that altering the course of metabolic syndrome reverses the course of erectile dysfunction. The Massachusetts Male Aging Study, a large random-sample cohort study involving patients who were interviewed in 1987–1989 and re-interviewed in 1995–1997, was one of the first to demonstrate that lifestyle factors played a key role in development of erectile dysfunction. The survey was able to demonstrate that smoking, hypertension, obesity, composite coronary risk score, physical activity, and fat intake were all correlated with the development of ED [55]. This pattern was again demonstrated in the Health Professionals Follow-up Study of erectile dysfunction in a cohort of 22,086 health care professionals surveyed in 1986 and again in 2000 [9]. This study was able to demonstrate that obesity (RR = 1.9; 95 % CI 1.6–2.2) and smoking (RR = 1.5; 95 % CI 1.3–1.7) significantly increased the risk of developing ED and that physical activity (RR = 0.7; 95 % CI 0.7–0.8) decreased the risk of developing ED in the follow-up survey ($P < 0.05$). In nationally representative managed care claims database including 28 million patients, only 32 % of the 27,325 patients who were identified as having erectile dysfunction had no comorbid conditions (DM, hypertension, hyperlipidemia, or depression) [169]. In a meta-analysis of 8 separate observational studies involving 12,067 participants, metabolic syndrome was associated with a 2.6-fold increased risk of having ED ($P < 0.0001$); most of the individual components of metabolic syndrome was also associated with increased risk of ED [19].

In patients with metabolic syndrome and ED, treatment of metabolic syndrome (via either pharmacotherapy or lifestyle changes) has been shown to improve metabolic parameters and erectile parameters. In a RCT of 209 patients with ED and

metabolic syndrome, patients randomized to aggressive lifestyle intervention vs. control (patients provided general health information) for 2 years, there were significant improvements in multiple parameters of metabolic syndrome as well as increased prevalence of patients with no ED [49]. Normal erectile function on the IIEF-15 survey increased from 34 to 56 % after 2 years in the intervention group compared to 36 % and 38 % in the control group ($P<0.015$). In a RCT of patients randomized to a Mediterranean diet vs. a control diet for 2 years, there was a 3.7 point increased in the IIEF-5 score compared to 0.3 points for control ($P<0.015$) [48] In a RCT of 59 men with stable CHF in sinus rhythm, patients who underwent cycle ergometer exercise training for 8 weeks had significant improvements in the sexual activity profile assessment (SAP) score and quality of life compared to the no changes from the control group [14]. In a meta-analysis of 4 RCTS looking at effect of lifestyle modifications on IIEF scores in patients with ED, an average increase of 2.4 points (95 % CI: 1.2–3.6) was observed [69]. In a meta-analysis of 11 RCTs, use of statins resulted in a 3.4 point increase (95 % CI: 1.7–5.0) in IIEF vs. control [91], which is about half to a third of that of tadalafil (5.2–8.3) and similar to that of lifestyle changes (2.4–3.1) [25, 48, 69].

With the prevalence of metabolic syndrome increasing in both the young and elderly population, its role in ED cannot be ignored and should be addressed at the initial evaluation and treatment.

Erectile Dysfunction and Hypothyroidism

Other disorders are less common such as thyroid disorders. While data are limited regarding thyroid disorders, however a recent study looked at 48 adult men, 34 with hyperthyroidism and 14 with hypothyroidism [26]. The mean age of the enrolled subjects was 43.2 years old. In hyperthyroid men, the prevalence of hypoactive sexual desire (HSD), delayed ejaculation (DE), premature ejaculation (PE) and ED was 17.6, 2.9, 50, and 14.7 %, whereas in hypothyroid men, the prevalence of HSD, DE, and ED was 64.3 % and the prevalence of PE was 7.1 %. After thyroid hormone normalization in hyperthyroid subjects, PE prevalence fell from 50 to 15 %, whereas DE was improved in half of the treated hypothyroid men. Ejaculation latency time doubled after treatment of hyperthyroidism from 2.4 ± 2.1 to 4.0 ± 2.0 min ($p<0.05$) and declined significantly in hypothyroid men from 21.8 ± 10.9 to 7.4 ± 7.2 ($P<0.01$). Since the average age in this study was only 43.2, the results may not be fully translatable to the older men.

Erectile Dysfunction and Testosterone

Aside from DM, various hormonal problems in the aging male affect sexual desire, erections and ejaculation [138]. The most relevant of these hormonal issues in men is low testosterone (T). T deficiency (also known as hypogonadism) in aging men is

a condition associated with decreased sexual satisfaction and a decline of general well- being [138]. The definition of hypogonadism is as follows [20]: clinical syndrome that results from failure of the testis to produce physiological levels of testosterone (androgen deficiency) and a normal number of spermatozoa due to disruption of one or more levels of the hypothalamic-pituitary-testicular axis.

Abnormalities of the hypothalamic-pituitary-testicular axis at the testicular level cause primary testicular failure, whereas central defects of the hypothalamus or pituitary cause secondary testicular failure [20]. Hypogonadism also can reflect dual defects that affect both the testis and the pituitary. Primary testicular failure results in low testosterone levels, impairment of spermatogenesis, and elevated gonadotropin levels. Secondary testicular failure results in low T levels, impairment of spermatogenesis, and low or low-normal gonadotropin levels. Combined primary and secondary testicular failure results in low T levels, impairment of spermatogenesis, and variable gonadotropin levels, depending on whether primary or secondary testicular failure predominates [20].

Studies have demonstrated that serum T levels decrease at a rate of about 1 % per year after the age of 30 years [75, 112]. Harman et al. [75] measured T and sex hormone-binding globulin (SHBG), by radio immuno assay in stored samples from 890 men in the Baltimore Longitudinal Study on Aging. The authors observed significant, independent, age-invariant, longitudinal effects of age on both T and free T index (free T index = T/SHBG), with an average change of −0.124 nmol/L/year of T and −0.0049 nmol T/nmol SHBG/year of free T index. T, but not free T index, also decreased with increasing body mass index. Use of beta-blocking drugs was associated with higher T and higher free T index levels. Using total T criteria, the incidence of hypogonadal T levels increased to about 20 % of men over 60, 30 % over 70 and 50 % over 80 year of age. These percentages are even greater percentages when free T index criteria were employed.

Importantly, recent data has suggested that lower serum testosterone levels are associated with morbidity and mortality [175]. These authors used a clinical database to identify men older than 40 years with repeated T levels obtained from October 1, 1994, to December 31, 1999. A low T level as defined as total T level ≤ 250 ng/dL (≤8.7 nmol/L) or a free T ≤ 0.75 ng/dL (≤0.03 nmol/L). Men were classified as having a low T level (n = 166 [19.3 %]), an equivocal testosterone level (equal number of low and normal levels) (n = 240 [28.0 %]), or a normal T level (n = 452 [52.7 %]). The risk for all-cause mortality was estimated using Cox proportional hazards regression models, adjusting for demographic and clinical covariates over a follow-up of up to 8 years. T levels differed significantly between the three groups. Men with low T levels were older, had a greater BMI, and greater prevalence of DM compared with men with normal T levels. Men with equivocal T levels had a greater BMI than men with normal T levels. The data demonstrated that mortality in men with normal T levels was 20.1 % (95 % confidence interval [CI]: 16.2–24.1 %), 24.6 % (95 % CI: 19.2–30.0 %) in men with equivocal T levels and 34.9 % (95 % CI: 28.5–41.4 %) in men with low T levels (Fig. 12.4). After adjusting for age, medical morbidity, and other clinical covariates, low T levels continued to be associated with increased mortality (HR = 1.88; 95 % CI, 1.34–2.63; P < 0.001)

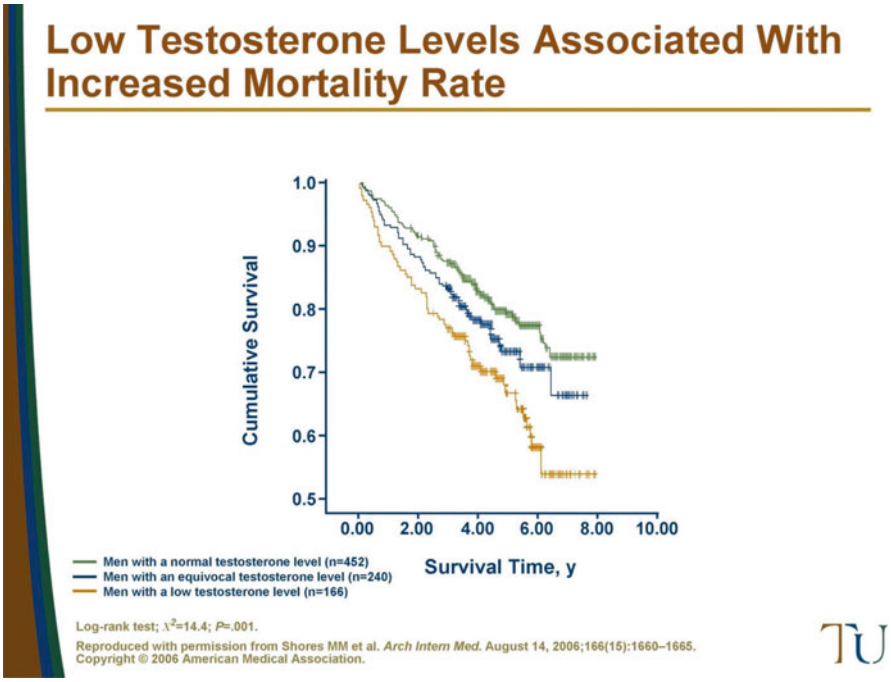

Fig. 12.4 A study was conducted to determine whether low testosterone levels are a risk factor for mortality in men 40 years of age or older. From the clinical database at the Veterans Affairs Puget Sound Health Care System, 858 male veterans who had repeated measurement of testosterone levels and no history of prostate or testicular cancer or antiandrogen treatment were identified. Testosterone levels were categorized as low if total testosterone was <250 ng/dL or free testosterone was <0.75 ng/dL. Testosterone levels were low in 166 men (19.3 %), equivocal (equal number of low and normal levels) in 240 men (28 %), and normal in 452 men (52.7 %). Cox proportional hazards regression models, adjusted for demographic and clinical covariates over an 8-year follow-up period, were used to compare differences in survival times between men with low, equivocal, and normal testosterone levels. As illustrated by the Kaplan-Meier survival analysis, survival times were shorter in men with low or equivocal testosterone levels than in those with normal testosterone levels. All-cause mortality was 34.9 % in men with low testosterone levels, 24.6 % in men with equivocal testosterone levels, and 20.1 % in men with normal testosterone levels (Adapted with permission from Shores et al. [175], Copyright © 2006 American Medical Association)

while equivocal testosterone levels were not significantly different from normal testosterone levels (HR = 1.38; 95 % CI, 0.99–1.92 %; P = 0.06).

A decline in serum T in the aging male is directly associated with a loss of sexual desire and erectile dysfunction [79, 206]. The authors in the EMAS study group surveyed a random population sample of 3369 men between the ages of 40 and 79 years at eight European centers (We et al. 2010). Levels of total testosterone were measured in morning blood samples by mass spectrometry, and free T levels were calculated with the use of Vermeulen's formula. Data were randomly split into separate training and validation sets for confirmatory analyses. In the training set,

symptoms of poor morning erection, low sexual desire, erectile dysfunction, inability to perform vigorous activity, depression, and fatigue were significantly related to the testosterone level. Increased probabilities of the three sexual symptoms and limited physical vigor were discernible with decreased testosterone levels: ranges, 8.0–13.0 nmol per liter [2.3–3.7 ng per milliliter] for total testosterone and 160–280 pmol per liter [46–81 pg per milliliter] for free testosterone. However, only the three sexual symptoms had a syndromic association with decreased T levels. An inverse relationship between an increasing number of sexual symptoms and a decreasing T level was observed. These relationships were independently confirmed in the validation set, in which the strengths of the association between symptoms and low T determined the minimum criteria necessary to identify late-onset hypogonadism. Late-onset hypogonadism can be defined by the presence of at least three sexual symptoms associated with a total testosterone level of less than 11 nmol per liter (3.2 ng per milliliter) and a free testosterone level of less than 220 pmol per liter (64 pg per milliliter).

Mechanism of Hypogonadism and Erectile Dysfunction

The effects of hypogonadism on male sexual desire seem to be well established [11]. The true contribution of hypogonadism to erectile and ejaculatory function is the subject of intense debate. It is postulated that penile erectile tissue possesses high concentrations of locally synthesized androgens and that testosterone-dependent functions are not a reflection of circulating androgen levels [17]. In several animal studies, testosterone deprivation changed the response and structural functionality of erectile tissue [188]. Testosterone is required for adequate function of nitric oxide synthase, which produces nitric oxide necessary for relaxation of cavernosal endothelial and corporeal smooth muscle resulting in erection [210]. Penile erection can also be mediated through a non-nitric oxide dependent pathway with the stimulation of cyclic AMP synthesis [119, 153]. Testosterone has also been shown to inhibit detrusor muscle contractions and thus lower testosterone levels may contribute to unstable function of the detrusor muscle and LUTS, especially in men with BPH [72].

Lower levels of testosterone also play a significant role in decreasing muscle mass, increasing fat mass, and weaker bone density as men age. Free testosterone has been shown to be the best predictor of loss of muscle mass and strength in the New Mexico Aging Process Study [146]. Sarcopenia eventually leads to frailty and subsequent functional deterioration as well as a substantial decrease in sexual functioning. Objectively, this is measured by unintentional weight loss, exhaustion and fatigue, general muscle weakness and lower sexual appetite. In additional to androgen, other factors including age, caloric intake, and physical activity all play different roles in the pathophysiology of frailty and decreased sexual functionality [122]. In longitudinal studies, the combination of loss of hormones such as testosterone and insulin-like growth factors (IGF-1) and increase in cytokines like tumor

necrosis factor (TNF-α) and interleukins (IL-6) provide the mechanism for the lost muscle mass and strength [122]. There is a direct effect of testosterone on osteoblasts contributing to increased bone mineral density [16]. However, the exact interactions between these hormones and their receptor activity and how further pathways contribute to muscle decline and higher rates of hip fractures are not well understood.

With respect to hypogonadism, decreased energy levels and impaired sexual performance were the two most important quality-of-life issues for older men in a recent study [31]. Dacal et al. [31] demonstrated lowering testosterone medically in patients with prostate cancer on androgen deprivation resulted in a large deterioration of quality of life [132]. This encompasses not only the lower physical and sexual activity in older adults, but also poorer cognition, less coordination, and satisfaction with functionality [31].

Lower testosterone has been correlated with more severe atherosclerotic changes and increased intima media thickness [41, 140]. Low-dose supplemental testosterone has been shown to decrease the incidence of exercise-induced myocardial infarction and ST depression in men with chronic stable angina [47, 121]. It can be inferred from these studies that testosterone may contribute to a beneficial effect on the cardiovascular system.

Yet, in spite of these data, a recent meta-analysis conducted on behalf of the Agency for Healthcare Research and Quality, revealed that the efficacy of hormonal treatments and the value of hormone testing in men with ED were inconclusive [187].

Testing for Males in Erectile Dysfunction

The paradigm has shifted in the field of male ED, and specifically ED in the aging male, such that the presumptive diagnosis is that the disease is either partly or fully organic in etiology. Historical tests to assess nocturnal erections, such as the snap-gauge and nocturnal penile tumescence testing have fallen by the wayside and are no longer used by most clinicians. Penile duplex Doppler ultrasound is used in conjunction with a penile injection of a vasoactive agent to induce an erection. This test is performed by select clinicians (urologists or radiologists) to assess the penile arterial tree and the penile capacity to trap blood under conditions that mimic an erection. Other tests are available as well (Table 12.8, from [201]), and are utilized for select patients. In light of the fact that most clinicians and patients move forward with oral treatment of their ED irrespective of the etiology of the ED, the utility of these tests for the older male with ED is questioned. Nonetheless, the penile duplex Doppler is quite helpful in defining the cause of the ED when used under the appropriate conditions [110]. Thus, the diagnosis of male erectile dysfunction is made predominately on the history, with confirmatory testing limited to specific patients.

Testing for hypogonadism should be relatively simple. The diagnosis is made based upon the presence of symptoms, such as low libido, fatigue, and erectile

Table 12.8 List of diagnostic tests for erectile dysfunction

Diagnostic tests for erectile dysfunction
Nocturnal penile tumescence and rigidity (NTPR) using Rigiscan®
Vascular studies
Intracavernous vasoactive drug injection
Duplex ultrasound of the cavernous arteries
Dynamic infusion cavernosometry or cavernosography (DICC)
Internal pudendal arteriography
Neurologic studies (e.g., bulbocavernosus reflex latency, nerve conduction studies)
Endocrinology studies
Specialized psychodiagnostic evaluation

Adapted with permission from the *EUA guidelines of erectile dysfunction* Wespes et al. [201]

dysfunction, combined with a serum T ≤ 300 ng/dl [20]. Mass screening of the population for low T is discouraged. While at face value this diagnosis should be relatively straightforward, the entire disease state, including the diagnosis has been the subject of recent debate. The assay to diagnose low T has been scrutinized and is under intense review [192]. As it stands now, many of the assays in current use may fall by the wayside. Next, the lower level of normal, 300 ng/dl, has been discussed in depth and is not universally accepted (84). Currently, many commercial labs have lower thresholds, e.g., 200 ng/dl, 242 ng/dl, 262 ng./dl. Additionally, there has been discussion that hypogonadism in older men (age > 65), is a distinct disease state, dissimilar to hypogonadism in younger men (Age < 50) [112, 198]. While there are many advocates supporting the position that hypogonadism is highly prevalent in this older age group [203], others suggest that the actual incidence is quite low [206]. The Institute of Medicine published a very thorough review of this topic and stated the following, "Hypogonadism occurs in men of various ages, and most clinical studies of the therapy so far have been in younger hypo-gonadal men. Less is known about the potential beneficial or adverse effects of testosterone therapy in older males and there have been concerns regarding prostate outcomes" [78]. Controversy abounds in this field. Further, the FDA recently issued a warning about the diagnosis of hypogonadism altering the definition of age-related hypogonadism [51, 53].

Treatment Options of Erectile Dysfunction

The etiologies of erectile dysfunction in an elderly male are countless. Initial treatment should always be aimed at searching for an underlying cause and reversing that pathophysiology if possible. For example, as mentioned above, if the patient has ED secondary to metabolic syndrome, lifestyle and pharmaceutical changes should be part of the treatment plan. After reversible pathophysiology have been explored, there are many treatments for male ED including oral pills, injection of vasoactive agents into the corpus cavernosum, vacuum device therapies, intra urethral therapies, and

surgical options [119, 170]. These options, regardless of etiology, may provide a satisfactory sexual experience for the patient and his partner. However, the success rate of specific treatment options vary depending on cause [119].

Oral therapies include the phosphodiesterase-5 inhibitor (PDE5I) class of medications (sildenafil, vardenafil, and tadalafil). PDE5 is found in trabecular smooth muscle and it catalyzes the degradation of cGMP, which elevates cytoplasmic calcium concentrations leading to smooth muscle contraction. PDE5 inhibitors block this mechanism for improvement in erectile function [64, 119]. These classes of medication can substantially and rapidly decrease blood pressure in patients who are concurrently taking nitrates and are therefore contraindicated in patients taking any form of nitrate therapy. Historically, the PDE5I have been taken orally as on demand medications. Tadalafil has changed this landscape; Tadalafil has a half-life of 17.5 h [25] and provides a 36-h activity window while the other two drugs in the class indicate 4–8 h therapeutic windows. There are ample short –term data which support the safety and efficacy of tadalafil [22]. RCTs (typically $\leq$12 weeks), indicate that PDE5Is were more effective than placebo in improving sexual intercourse success (69.0% vs. 35.0%) [22, 187]. The proportion of men with improved erections was significantly greater among those treated with PDE5I (range: 67.0–89.0%) than with placebo (range: 27.0–35.0%) [31]. Interestingly, improvements in erectile function are gauged, in some studies, by an improvement in the IIEF score, among several other questionnaires [22, 64, 119, 187]. The improvement in erectile function is proportional to dose of the drug taken. Data suggest that many men drop out of therapy approximately 1 year after starting therapy. It is unclear if this is due to drug cost (as many insurance plans do not cover this oral therapy), side effects, lack of efficacy, partner issues or combinations thereof [70]. Side effects are mild, limited, well tolerated and usually do not cause the patient to cease therapy. The most common side effects include headache, rhinitis, dyspepsia, facial flushing, myalgia and back pain [119, 187].

The efficacy and safety of oral sildenafil (Viagra) for treating ED in elderly men (aged $\geq$65) was reported in a 2001 review and a 2002 review [57, 195]. In Wagner et al. [195], the authors analyzed data obtained from five double-blind, placebo-controlled studies of the efficacy and tolerability of oral sildenafil taken as required (but not more than once daily) over a 12-week to 6-month period. Two subgroups were evaluated: (i) elderly patients with ED of broad-spectrum etiology (n=411), and (ii) elderly patients with ED and diabetes (n=71). Efficacy was assessed using a global efficacy question, IIEF question 3 and 4, and the IIEF sexual domain questions. All efficacy assessments indicated that sildenafil significantly improved erectile function both in elderly patients with ED of broad-spectrum etiology and in elderly patients with ED and diabetes. The most common adverse events were mild-to-moderate headache, flushing, and dyspepsia. The rates of discontinuation due to adverse events were low and were comparable to the rates with placebo.

Beyond these oral agents, nonpharmacologic entities for treatment include intracavernosal injections; intraurethral suppositories, penile implants, vascular reconstruction, and vacuum erection pump devices. All invasive treatment options can be limited by patient age, fear of injections/surgery, lack of spontaneity, risk for penile injuries, priapism and fibrosis, and pain [155]. For the optimal treatment plan, it

usually takes a combination of lifestyle changes, psychosocial counseling, sexual techniques, good patient-physician communication, and appropriate treatment modality.

A more invasive surgical option is penile arterial bypass surgery, which has been shown to have long-term success in a select group of young, healthy patients with no vascular risk factors and pure cavernous arterial insufficiency [142]. However, this is typically irrelevant in elderly patients because their atherosclerosis or DM make then poor candidates for revascularization surgery.

Penile injections work well in 300 older men, mean age 67.1, with erectile dysfunction of organic origin were treated with penile injections [155]. Among the patients, 180 underwent first trial with injection of prostaglandin E1 (PE). Further on these 180 patients and another 120 (in total 300 patients) were treated with a triple combination of papaverine hydrochlorate, phentolamine messylate and prostaglandin E1 (PPR). The number of responders to the injection of either PE alone or the drug combination was recorded. These authors observed a statistically significant association between the results obtained after the injection of PPR as compared to PE (chi^2 with 2 d.f.: 34.666; $P \leq 0.001$). A functional erection was obtained in 224/300 (74.7 %) after the injection of PPR as compared to 87/180 men (48.3 %) treated with PE. The average volume of PPR necessary to obtain a functional erection was 0.35 ± 0.14 ml whereas that of PE was 1.3 ± 0.3 ml. Thus, it appears that both the PE and PPR yielded functional erections in a significant number of older men with ED. The limitation of these injections is that they require manual dexterity and can cause penile pain, causing many people to drop out [119].

Vacuum pumps are rather cheap and non-invasive devices that can be used to obtain an erection with no systemic side effect. However, this device is unnatural and can cause bruising and numbness of penis from compression [119].

With respect to the implantation of penile prosthesis in older men, data suggest that this is a viable option. Al-Najar et al. [5] studied 174 patients who received, for the first time, a penile prosthesis between 1990 and 2007. Among these, 35 patients were ≥ 70 years old at time of prosthesis implantation. Of those patients, 18 were still alive at the time of follow-up. Using a telephone survey, patients were asked to answer the Erectile Dysfunction Inventory of Treatment Satisfaction (EDITS) and IIEF. 15 of 18 patients were either very or somewhat satisfied (83 %). Eleven out of fifteen (73 %) patients were using their prosthesis regularly. The mean IIEF and EDITS scores were 21.80 and 75.20, respectively. Based on this small study, that a penile prosthesis is a viable option for the older male. This procedure is typically reserved for patients who failed medical therapy because of the risks of anesthesia and surgical complications in patients who are typically non-ideal operative candidates.

Daily Oral PDE5I Therapy for Male ED

Historically, oral PDE5I were taken on an as-needed basis. This meant that the man would take the oral PDE5I prior to the anticipated sexual encounter. With Tadalafil, both 2.5 and 5 mg, improved erectile function may be achieved with a standing

daily dosage [3, 152, 171]. While no specific studies have been performed in aging men, older men were included in clinical trial that examined daily dosing and appeared to receive benefit from daily tadalafil. As is seen in this dataset, the efficacy and safety of tadalafil, dosed once a day for the treatment of erectile dysfunction, was assessed in a randomized, double-blind, placebo-controlled, parallel-design study at 15 US centers. Following a 4-week treatment-free run-in period, patients (18 years of age) were randomly assigned to 24 weeks treatment with tadalafil 2.5 mg, tadalafil 5 mg or placebo. Primary efficacy endpoints were change at 24 weeks IIEF – EF domain score and mean per-patient percentage 'yes' responses to SEP diary questions 2 and 3. Tadalafil significantly improved erectile function compared with placebo for all three co-primary efficacy endpoints. Few patients discontinued because of adverse events (2.1 %, placebo; 6.3 %, tadalafil 2.5 mg; 4.1 %, tadalafil 5 mg). Common treatment-emergent adverse events were nasopharyngitis, influenza, viral gastroenteritis and back pain. Tadalafil 2.5 mg and 5 mg, dosed once a day was well tolerated and significantly improved erectile function.

Daily dosing with tadalafil has changed the ED treatment paradigm. Evidence for improvement in various outcome measures as seen in Seftel et al. [171]. After a 4-week run-in phase, participants were randomized to receive either tadalafil 5 mg (N = 264) or placebo (N = 78) for 12 weeks. Participants and partners were more satisfied based on the treatment satisfaction domain of Sexual Life Quality Questionnaire (THX) with tadalafil (75 % and 73 %, respectively) versus placebo (51 % and 55 %, respectively, $P < 0.001$). An efficacy study of tadalafil (5 mg once daily) for treating erectile dysfunction included sexual satisfaction and psychosocial outcome measures such as THX, Self-Esteem And Relationship (SEAR) questionnaire, SEP4; hardness satisfaction, SEP5; overall satisfaction, intercourse satisfaction (IS) and overall satisfaction (OS) domains IIEF, and partner SEP question 3 (pSEP3). Statistically significant improvements in SEAR, IS, OS, SEP5 and pSEP3 for tadalafil compared with placebo ($P < 0.001$) correlated with erectile function improvement (assessed by change in IIEF-EF score). Tadalafil significantly improved treatment and sexual satisfaction, while improving multiple outcomes measured by SEAR. Daily tadalafil for the treatment of male ED was FDA approved in 2008 and is a viable option for the treatment of male ED [43].

Effects of Treating Male ED on the Partner/Relationship

Data has emerged that treatment of male ED has led to varying degrees of improved partner satisfaction as well. A retrospective analysis included data pooled from 2 multicenter, randomized, double-blind, placebo-controlled trials that included 505 couples (tadalafil, N = 373; placebo, N = 132) in which the men received tadalafil 5 mg once daily or placebo for 12 weeks [3]. Individual SEP diaries were completed independently by the male subject and his female partner after each sexual intercourse attempt. The mean per-subject/per-partner percentage of

"yes" responses to SEP diary questions and agreement between subjects' and partners' responses was assessed. Subjects and partners in the tadalafil-treated group reported significantly greater improvements in the man's ability to achieve some erection, vaginal penetration, and overall sexual satisfaction compared with placebo ($P < 0.001$). For all intercourse attempts, the mean per-couple agreement for those in the tadalafil and placebo groups, respectively, was high for erection achievement (99.0 and 96.6 %), vaginal penetration (98.6 and 97.4 %), and overall satisfaction (84.3 and 82.8 %). These authors concluded that tadalafil 5 mg taken once daily as treatment for ED improved overall satisfaction for men and their female partners and that there is high concordance among couples in their responses to the man's treatment for ED.

One hundred heterosexual couples in stable relationships, with male partners having ED based on the erectile function subscale of the IIEF, were randomly assigned to receive sildenafil or tadalafil for a 12-week phase, followed by another 12-week period using the alternate drug [28]. Male and female participants completed sexual event diaries during both study phases, and the female participants were interviewed at baseline, midpoint, and end of study. Primary outcome data were the women's final interviews during which they were asked which drug they preferred and their reasons for that preference. A total of 79.2 % of the women preferred their partners' use of tadalafil, while 15.6 % preferred sildenafil. Preference was not affected by age or treatment order randomization. Women preferring tadalafil reported feeling more relaxed, experiencing less pressure, and enjoying a more natural or spontaneous sexual experience as reasons for their choice. Mean number of tablets used, events recorded, events per week, and days between events were not significantly different during each study phase.

New Concept: Daily Tadalafil for Both ED and BPH/LUTS

As men age, the prostate enlarges and produces a variety of symptoms termed lower urinary tract symptoms (LUTS). LUTS is characterized by urinary frequency, urgency, weak stream, and nocturia [1]. LUTS is prevalent in more than half of men over the age of 50 years. BPH and LUTS significantly decrease quality of life in aging men and may worsen to acute urinary retention requiring emergency care. Epidemiologic studies indicate a strong association between lower urinary tract symptoms (LUTS) and male sexual dysfunction (ED and ejaculatory dysfunction) suggesting a common pathophysiologic theme [21, 154]. In addition, both erectile and ejaculatory disorders appear more frequently in men in conjunction with symptoms of moderate to severe LUTS [21, 154]. Although the exact mechanisms in regard to how LUTS affect sexual function are not clear, there appears to be a direct relationship between the two. This is especially evident when sexual problems are encountered or exacerbated by management of LUTS (Fig. 12.5) [154]. The Multinational Survey of the Aging Male (MSAM-7) was conducted in the United States and 6 European countries to systematically investigate the relationship

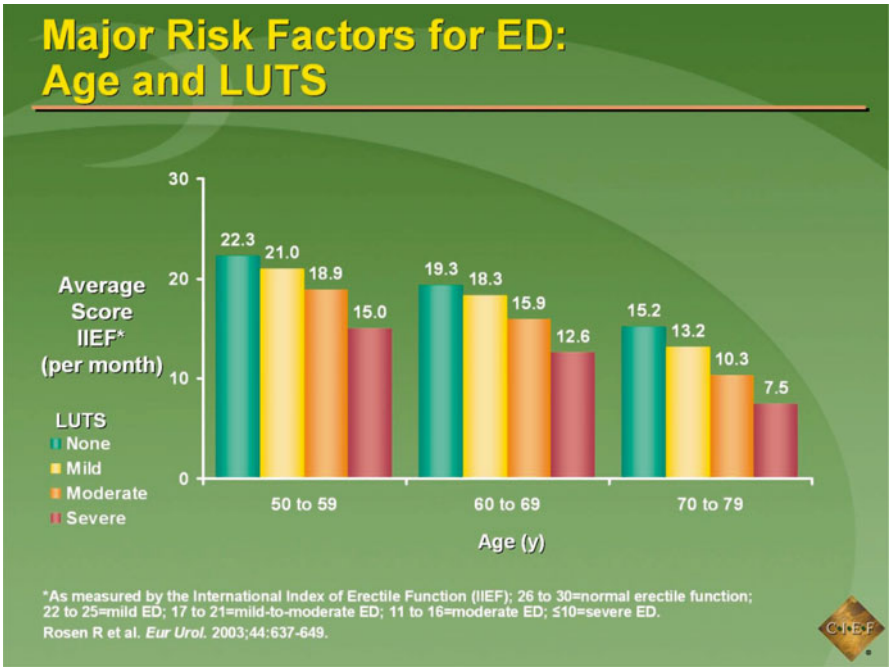

Fig. 12.5 Data shows average score for Erectile Function (as measured by IIEF) in each age group amongst men without LUTS (*left column*). As expected, a clear decline in Erectile Function with increasing age is observed. Within each age group, the average score for Erectile Function (*IIEF*) decreases significantly with increasing severity of LUTS. The same relationship hold true for ejaculatory dysfunction (Adapted from Rosen et al. [154])

between LUTS and sexual dysfunction in older men aged 50–80 years [154]. LUTS and sexual function were assessed using validated symptom scales, including the International Prostate Symptom Score (IPSS) for LUTS, and the Danish Prostatic Symptom Score and the IIEF for sexual function. A total of 12,815 surveys were included in the analysis. The men's self-ratings of erectile function were stratified according to the severity of LUTS. As expected, there was a gradual worsening of erectile function with increased age. However, within each age group, there was a clear, statistically important relationship between the severity of LUTS and erectile capacity: as LUTS worsened, so did erectile function. Moreover, the relationship between sexual problems and LUTS was independent of comorbidities such as diabetes, hypertension, cardiac disease, and hypercholesterolemia.

There was a clear age-related decline in male sexual function, both erectile function and ejaculatory function, seen with aging. The decline in sexual function with aging was exacerbated by worsening LUTS. For example (Fig. 12.5), if a man in the age bracket 50–59 has no LUTS, his erectile function score was quite good at 22.3. As the LUTS take effect, the worsening of the LUTS symptoms now demonstrated that the same man has a worsening of his erectile function. Indeed, with moderate LUTS, the erection score drops to 18.9, a 15 % decline in erectile

function (Fig. 12.5). The clinical implications of these recent studies suggest that a man who presents with LUTS should be carefully evaluated for the presence of sexual problems and vice versa.

The possible pathophysiologic mechanistic relationship between LUTS and ED is the subject of intense investigation [139]. One plausible common mechanism is that both organs (the prostate and the penis) contain phosphodiesterase type 5, and either upregulation of the intrinsic PDE5 enzyme or loss of intrinsic PDE5 inhibitor protein may cause exacerbation of prostate smooth contraction and penile corpus cavernosum contraction. Excessive contraction prevents the relaxation needed for penile erection and the prostate relaxation needed for the patient to void. The PDE5 and PDE5 inhibitor mechanisms are well elucidated for the penile corpus cavernosum smooth muscle [119], but are not as clearly defined in the prostate. cGMP and PDE5 have recently been identified in human and rate prostate via immunohistochemistry, mRNA, and western blot [133, 139, 190]. Additionally, PDE5 inhibitors have been shown to relax prostate tissue in vitro [139, 191, 209].

Uckert et al. [190] performed the following experiments. Using the organ bath technique, the effects of increasing concentrations (1 nM to 10 microM) of the PDE5 inhibitors sildenafil, tadalafil, and vardenafil and the PDE4 inhibitors rolipram and RP 73401 on the tension induced by norepinephrine (NE, 40 microM) of prostate strip preparations were investigated. The accumulation of cGMP and cAMP in response to drug exposure was determined by radioimmunoassays, The tension induced by NE was dose dependently reversed by the drugs with the following rank order of efficacy: tadalafil > RP 73401 > rolipram > vardenafil > sildenafil. The maximal reversion of tension values ranged from 52.3 % (tadalafil) to 17 % (sildenafil). Of the PDE inhibitors, only tadalafil induced a 50 % reversion of the initial tension. The most prominent enhancement in tissue cyclic adenosine monophosphate was registered in response to RP 73401 (11-fold), and cGMP levels were significantly elevated by tadalafil, vardenafil, and sildenafil (28-fold, 12-fold, and 3-fold, respectively).

Zhang et al. [209] investigated the effect of testosterone (T) on smooth muscle (SM) contractile and regulatory signaling pathways including PDE5 expression and functional activity in prostate in male rats (sham-operated, surgically-castrated and castrated with T supplementation). In vitro organ bath studies, real-time RT-PCR, Western blot analysis, and immunohistochemistry were performed. PDE5 was immunolocalized exclusively in the prostate stroma. The PDE5I zaprinast significantly increased prostate strip relaxation to the nitric oxide donor sodium nitroprusside (SNP) in control but not castrated rats. But SNP alone was more effective on castrated rats, comparable with sham treated with SNP plus zaprinast. T supplementation prevented or restored all above changes, including SNP and zaprinast in vitro responsiveness. These data show that T positively regulates PDE5 expression and functional activities in prostate, and T ablation not only suppresses prostate size but also reduces prostatic SM contractility, with several potential SM contraction/relaxation pathways implicated. Zaprinast findings strongly suggest a major role for PDE5/cGMP in this signaling cascade. These data support PDE5 inhibition as a potential mechanism for treatment of BPH.

Treatment of LUTS used to be centered on oral α blockers and 5-α reductase inhibitors [109]. α blockers include such drugs as doxazosin, terazosin, tamsulosin, alfuzosin and silodosin. 5-α reductase inhibitors include drugs such as finasteride and dutasteride. While both of these medications effectively work to reduce LUTS and BPH symptoms, they may cause sexual dysfunction such as decreased libido, erectile dysfunction, or ejaculatory disorders [97, 161]. This makes both classes of drugs less than ideal in treating patients with ED and BPH/LUTS.

A recent development in the treatment of patients with BPH/LUTS and ED is the use of PDE5I to treat both problems at once. In double-blinded RCTs, many PDE5I's are efficacious at improving the IPSS, IIEF, and BII [60]. However, Tadalafil is particularly useful for this purpose because it has a long half-life of 17.5 h and requires once daily dosing. Tadalafil was recently approved in 2011 by the FDA for daily use for the treatment of both BPH/LUTS and ED [44]. Multiple double-blinded RCTs have that tadalafil can improve LUTS in a similar manner to α blockers and ED symptoms [39, 42, 147, 149, 158, 181]. Sildenafil (Fig. 12.6) [127] and vardenafil also improve BPH/LUTS symptoms but have not yet cleared the FDA regulatory hurdles for the BPH indication [60, 127].

Multiple high-quality double-blinded RCTs have been conducted comparing PDE5I to placebo (Table 12.9). In terms of IPPS, all studies found a statistically significant improvement in patient treated with Tadalafil 5 mg dose or higher. The treatment vs. placebo standard mean difference (SMD) was 1.5–3.0 points ($p < 0.05$ for SMD). Tadalafil 2.5 mg daily was associated with a sub-optimal response. Patients who were initially given 2.5 mg daily in the open label trial (Donatucci et al. 2012) had IPSS improved by 3.1 points after 12 weeks if 2.5 mg

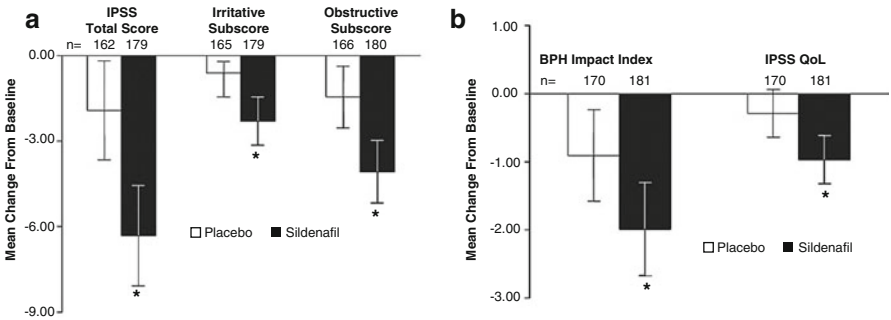

Fig. 12.6 Change in LUTS scores from baseline to end of treatment. Patients completed I-PSS irritative and obstructive subscales (**a**), and BPHII and I-PSS QOL question (**b**) at baseline and after 12 weeks of randomized treatment. Maximum I-PSS score is 35 points, maximum irritative subscore is 15 points and maximum obstructive subscore is 20 points. Maximum BPHII score is 13 points. I-PSS QOL question asks "If you were to spend the rest of your life with your urinary condition just the way it is now, how would you feel about that?" and it is scored on 0–6-point scale. Lower I-PSS and BPHII scores indicate fewer LUTS, less bother and better QOL. Greater decreases in LS mean scores on each set of questions indicate better treatment outcome. Data are shown as LS mean change with 95% CI. *Asterisk* indicates sildenafil change in LS mean score vs placebo change in score $p < 0.0001$ (Reproduced with permission from McVary et al. [127])

Table 12.9 Summary of randomized control trials of PDE-5I and their effect on BPH symptoms and erectile dysfunction

	Treatment	Δ IPSS	Δ BII	Δ Q_{max}	Δ IIEF	Other
Roehrborn et al. [158]	Placebo	−2.27	−0.83	1.21	2.20	
	Tadalafil 2.5 mg	−3.88*	−0.96*	1.41	5.59*	
	Tadalafil 5 mg	−4.87*	−1.4*	1.64	6.97*	
	Tadalafil 10 mg	−5.17*	−1.38*	1.58	7.98*	
	Tadalafil 20 mg	−5.21*	−1.45*	1.96	8.34*	
Porst et al. [149]	Placebo	−3.6	−1.3	n/a	2.0	
	Tadalafil 5 mg	−5.6*	−1.8*	n/a	6.7*	Improved CGI-I and PGI-I
Oelke et al. [147]	Placebo	−4.2	−0.9	1.2	2.1	No change in PVR, Bladder Cap, V_{void}
	Tamsulosin 0.4 mg	−5.7*	−1.5*	2.2*	1.7	
	Tadalafil 5 mg	−6.3*	−1.7*	2.4*	6.0*	Improved CGI-I and PGI-I
Egerdie et al. [42]	Placebo	−3.8	−1.2	n/a	1.2	
	Tadalafil 2.5 mg	−4.6	−1.6	n/a	5.2*	Improved CGI-I and PGI-I, SEP Q3
	Tadalafil 5 mg	−6.1*	−2.1	n/a	6.5*	Improved CGI-I and PGI-I, SEP Q3
Donatucci et al. (2012)	5 mg -open label	−5.0	−1.3	n/a	5.9	
Takeda et al. [181]	Placebo	−4.5	n/a	n/a	n/a	
	Tadalafil 5 mg	−6	n/a	n/a	n/a	Improved CGI-I and PGI-I

IPSS International prostate symptom score, *BII* change in BPH Impact Index, *IIEF* International Index of Erectile dysfunction

*Indicates $p < 0.05$

daily and subsequent improvement of another 2.5 points after the 1-year open label period in which they were given 5 mg daily. Patients who initially received 5, 10, or 20 mg had minimal changes in IPSS during the open label period (−0.2 to 0.8). Egerdie et al. [42] did not find a statistically significant change in IPSS in patients given 12 weeks of 2.5 mg but did find a significant improvement of 2.3 points in patients who were given 5 mg. IPSS storage sub-scores and voiding sub-scores were significantly higher when given 5 mg or more in all RCTs mentioned above. Several studies also found a significant difference in BII, CGI-I, and PGI-I scores between placebo and tadalafil doses 5 mg or higher [42, 147, 158, 181]. The IIEF-EF score was significantly improved at all dosages of tadalafil. Only 1 study [42] demonstrated a significant increase in Qmax (2.4 mL/h vs. 1.2 mL/h for placebo, $p < 0.05$). Of noted, the changes in IIEF, BII, and IPSS from baseline of patients receiving placebo is usually greater than the mean difference between

placebo and treatment group, suggesting that the thought of getting tadalafil itself strong impacts patients' perception of their symptoms.

Based on a recent meta-analysis the average IPSS improvement (not SMD compare to placebo) of α-blockers is −4 to −6 points after 3–9 months [6]. The average IPSS improvement of Dutasteride in the Combination of Avodart and Tamsulosin study after 15 months is −4.8 points [158]. The IPSS associated with Tadalafil is comparable to those values (See Table 12.9).

The most common side effects were headaches, dyspepsia, back pain, and nasopharyngitis [25]. In a pooled dataset from three major studies [25], >90 % of the side effects reported were of mild or moderate severity. The discontinuation rate in these studies was 4 % compared to 1.6 % in placebo-treated group. Based on these data, Tafalafil is safe to use in patient with BPH/LUTS and ED.

Evidence comparing PDE5-I and other BPH/LUTS medications is scarce. Oelke et al. [147] randomized patients to placebo (n = 172), tadalafil 5 mg daily (n = 171), or tamsulosin 0.4 mg daily (n = 168) for 12 weeks. IPSS significantly improved versus placebo after 12 weeks with tadalafil (−2.1; $p = 0.001$) and tamsulosin (−1.5; $p = 0.023$). Improvements were seen as early as 1 week in both tadalafil and tamsulosin (−1.5, $p < 0.01$). BPH Impact Index significantly improved versus placebo at first assessment (week 4) with tadalafil (−0.8; $p < 0.001$) and tamsulosin (−0.9; $p < 0.001$) and through 12 week (tadalafil −0.8; $p = 0.003$; tamsulosin −0.6; $p = 0.026$) (Fig. 12.7). The IPSS Quality-of-Life Index and the Treatment Satisfaction Scale-BPH improved versus placebo with tadalafil (both $p < 0.05$) but not with tamsulosin ($p > 0.1$). IIEF-EF improved versus placebo with tadalafil (4.0; $p < 0.001$) but not tamsulosin (−0.4; $p = 0.699$). Q_{max} increased significantly versus placebo with both tadalafil (2.4 ml/s; $p = 0.009$) and tamsulosin (2.2 ml/s; $p = 0.014$). Adverse event profiles were consistent with previous reports. This study was limited in not being powered to directly compare tadalafil versus tamsulosin. The data suggest that monotherapy with tadalafil or tamsulosin resulted in significant and numerically similar improvements versus placebo in LUTS/BPH symptoms and Q_{max}. However,

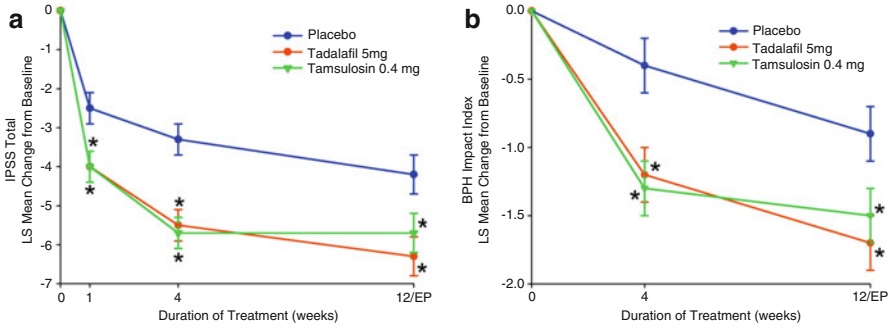

Fig. 12.7 Changes from baseline in (A) total International Prostate Symptom Score and (B) Benign Prostatic Hyperplasia Impact Index. Data represent the least squares mean change plus or minus standard error. *LS* least squares, *EP* end point, *ANCOVA* analysis of covariance.* $p < 0.05$ versus placebo based on ANCOVA (Reprinted with permission from Oelke et al. [147])

only tadalafil improved erectile dysfunction. Thus, daily tadalafil is a viable option for treatment of ED and BPH/LUTS.

Several studies have also studied whether implementation of Tadalafil in addition to α-blockers or 5-α-reductase inhibitors (5-ARI) provides additional benefits. Gacci et al. [60] performed a meta-analysis of RCTs that studied RCT α-blocker vs. α-blockers and PDE5I. A total of 5 RCTs studying a total of 216 men, all for 12 weeks, was included in the analysis. The meta-analysis concluded that combination therapy results in an additional improvement in IPSS (−1.85, 95 % CI: −3.73–0.00), IIEF (3.6, 95 % CI: 0.91–2.16), and Q_{max} (1.53, 95 % CI: 3.07–4.12) compared to α-blocker monotherapy. Side effects were mild and rarely resulted in termination of therapy in both arms. A meta-analysis of 5 RCTs involving 464 patients (277 in combination group) compared PDE5I alone vs PDE5I and α-blockers was conducted [208]. All studies were carried out for 12 weeks. Yan et al. concluded that combination therapy results in an additional improvement in IPSS (−4.21, $p<0.005$), IIEF (2.25, $p<0.05$), and Q_{max} (1.43, $p=0.007$) compare to monotherapy. Side effects were mild and rarely resulted in termination of therapy in both arms. In a double-blinded RCT, Casabe et al. [27] randomized 696 men to placebo/finasteride 5 mg vs. tadalafil 5 mg/finasteride 5 mg for 26 weeks. Inclusion criteria were age ≥45, IPSS ≥ 13, prostate volume ≥ 30 mL, Qmax between 4 and 15 ml/s, and 5-ARI-naive. Combination therapy resulted in a significant improvement in IPSS at 4 weeks (−4.0 vs −2.3, $p<0.001$), 12 weeks (−5.2 vs. −3.8, $p<0.001$), and 26 weeks (−5.5 vs. −4.5, $p<0.05$). Combination therapy resulted in a significantly greater change in IIEF at 4 weeks (3.7 vs −1.1, $P<0.001$), 12 weeks (4.7 vs 0.6, $P<0.001$), and 26 weeks (4.7 vs 0.0, $P<0.001$). Patients also had improved PGI-I ($p<0.05$) but not CGI-I scores with combination therapy. In another double-blinded RCT 695 men were randomized to placebo/finasteride 5 mg vs. tadalafil 5 mg/finasteride 5 mg for 26 weeks [69]. Inclusion criteria were age ≥45, BPH/LUTS ≥ 6 months, IPSS ≥ 13, 5-ARI-naïve, and prostate volume ≥ 30 mL. In men with and without ED, combination therapy resulted in a significant improvement in IIEF at 4 weeks, 12 weeks, and 26 weeks compare to finasteride/placebo. The OR of patients with ED achieving a minimal clinically important difference (MCID), defined as ≥ 4 in IIEF-EF score, was 5.32 at 4 weeks ($p<0.001$), 3.05 at 12 weeks ($p<0.001$), and 3.46 at 26 weeks ($p<0.001$). These RCTs provide evidence PDE5Is, when added to an a-blocker or 5-ARI, provide additional benefits to BPH-LUTS and ED.

Treatment of Hypogonadism: Aging Male with Testosterone

Treatment for men with symptomatic hypogonadism is testosterone supplementation. There are multiple methods of delivery including injectable, implantable pellets, buccal, transdermal patches, nasal spray and gels [118]. Although side effects exist, testosterone replacement therapy has been shown to improve muscle mass, energy levels, and bone strength. In older men with significant hypogonadism, testosterone treatment has been effective in enhancing the strength and maintenance of erections

[73, 99, 173, 174, 182]. In the absence of hypogonadism, testosterone supplementation has been shown to improve the response to sildenafil [173, 174]. Aversa et al. demonstrated that in patients with ED and low-normal androgen levels, short-term testosterone administration increased testosterone (total and free) levels and improved the erectile response to sildenafil likely by increasing arterial inflow to the penis during stimulation [7].

Controversy exists regarding the lower end of normal for hypogonadism along with the normal levels for the aging male. There is currently no golden standard for what defines hypogonadism in aging men [165]. Seftel et al. [167] attempted to provide guidance regarding the therapeutic targets for T replacement. Hypogonadal male subjects from the Testim phase 3 studies (total T ≤ 300 ng/dL, n = 406, mean age = 58) reporting one or more symptoms of low testosterone were randomized to T gel (50 mg/day and 100 mg/day), T patch, or placebo. Twenty-four-hour pharmacokinetic profiles for T were obtained. The 3 primary end points evaluated at 30 and 90 days were frequency of intercourse, nighttime erections per 7-day week, and change in sexual desire measured by the Likert-type scale and calculated as a mean daily score. At day 30, a significant increase in sexual desire was noted for those on 100 mg/day T gel vs. 50 mg/day T gel, T patch, and placebo (1.2 vs 0.4, 0.7, and 0.4, respectively). A significant increase in the frequency of nighttime erections was also noted for patients on 100 mg/day T gel vs. patients on 50 mg/day T gel or placebo (51 % vs 30 % vs 26 %). Finally, a significant increase in the frequency of intercourse was evidenced for those on 100 mg/day T gel vs. those on T patch or placebo (39 % vs 21 % vs 24 % respectively). Similar results were seen for 100 mg/day T gel at day 90 for sexual desire and nighttime erections vs placebo. These data demonstrate a clear relationship between restoring serum T concentrations and improvement in certain parameters of sexual function. We propose that threshold T levels are needed in order to significantly affect improvements in sexual functioning. This threshold level appeared to be approximately 400 ng/dL for nighttime erections, 500 ng/dL for sexual intercourse, and 600 ng/dL for sexual desire. In all 3 parameters, there was no significant difference in sexual function between the group of subjects with the lowest serum T levels (0–300 ng/dL) and the group of subjects with the next highest serum T level (300–400 ng/dL for nighttime erections, 300–500 ng/dL for sexual intercourse, and 300–600 ng/dL for sexual desire, P = 0.16) (Fig. 12.8) [167].

A recent multi-center RCT from the Testosterone Trials [178] evaluated the benefit of T on various aspects of men's health. This study looked at 790 men age 65 or older who had T level less than 275 ng/dL and at least one complaint regarding their sexual function, physical function, or vitality. Men were randomized to T get vs. placebo for 1 year. This study reported some benefits of Androgel (1 % T gel) for 1 year in terms of several self-reported measures of sexual function. The primary endpoint, PDQ-Q4 score, was 0.58 ($p < 0.001$) greater in the treatment vs. placebo group for men with sexual dysfunction complaints and 0.62 greater ($p < 0.001$) in all Testosterone trial participants. There were very limited benefits of T replacement in terms of physical function and vitality. There was no increased risk of cardiovascular or prostatic adverse events.

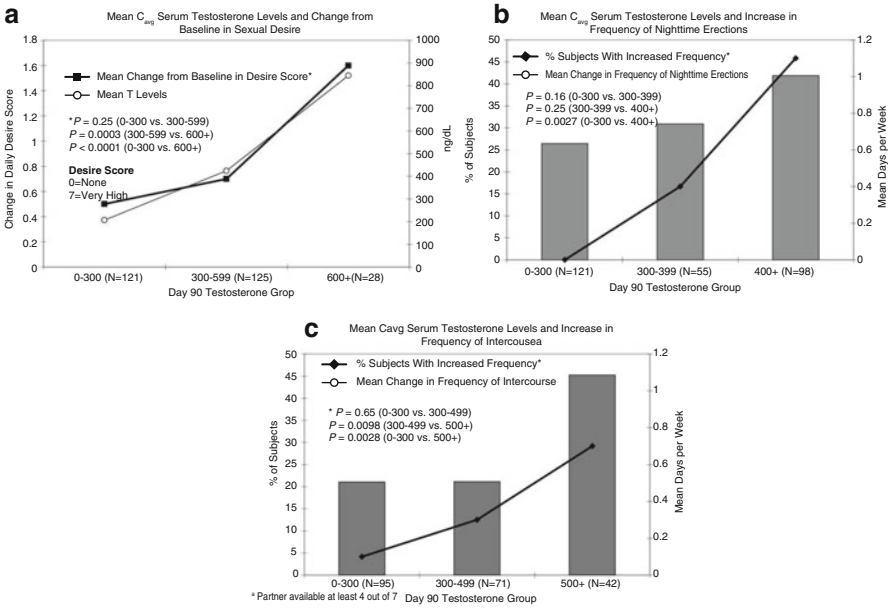
a
Mean C_{avg} Serum Testosterone Levels and Change from Baseline in Sexual Desire
Change in Daily Desire Score
ng/dL
Mean Change from Baseline in Desire Score*
Mean T Levels
*P = 0.25 (0-300 vs. 300-599)
P = 0.0003 (300-599 vs. 600+)
P < 0.0001 (0-300 vs. 600+)
Desire Score
0=None
7=Very High
0-300 (N=121)
300-599 (N=125)
600+(N=28)
Day 90 Testosterone Grop
b
Mean C_{avg} Serum Testosterone Levels and Increase in Frequency of Nighttime Erections
% of Subjects
Mean Days per Week
% Subjects With Increased Frequency*
Mean Change in Frequency of Nighttime Erections
P = 0.16 (0-300 vs. 300-399)
P = 0.25 (300-399 vs. 400+)
P = 0.0027 (0-300 vs. 400+)
0-300 (N=121)
300-399 (N=55)
400+ (N=98)
Day 90 Testosterone Group
c
Mean Cavg Serum Testosterone Levels and Increase in Frequency of Intercousea
% of Subjects
Mean Days per Week
% Subjects With Increased Frequency*
Mean Change in Frequency of Intercourse
* P = 0.65 (0-300 vs. 300-499)
P = 0.0098 (300-499 vs. 500+)
P = 0.0028 (0-300 vs. 500+)
0-300 (N=95)
300-499 (N=71)
500+ (N=42)
* Partner available at least 4 out of 7
Day 90 Testosterone Group

Fig. 12.8 Mean change from baseline for daily sexual desire score and mean C_{avg} (0–24 h) serum testosterone levels (ng/dL); percentage of subjects with increased frequency and mean change in frequency for nighttime erections and intercourse (Adapted with permission from Seftel et al. [167]) (**a**) daily sexual desire score, (**b**) frequency of night-time erections, and (**c**) frequency of intercourse in patients with mean Cavg (0–24 h) serum testosterone levels (ng/dL) of 0-300, 300-499, and 500+ after testosterone treatment

New formulations of T gels exist including Androgel 1.62 %, Testim, Axiron, and Fortesta. T patches (androderm) are available as is a buccal preparation, pellets (testopel) or standard intramuscular injections [89, 164, 184]. The buccal preparation is a twice daily application to the inner gum. The T pellets are subcutaneous injections usually performed at 3–4 month intervals. The standard intramuscular injections of T are injected by either the patient or caregiver at 1–3 week intervals. The reader is encouraged to evaluate each specific product to gain familiarity with these compounds.

The most T replacement side effects include local skin reactions to the gels, patches or IM injections, polycythemia, worsening of BPH/LUTS symptoms, increases in serum PSA, pedal edema, gynecomastia, transient oligo or azoospermia, and worsening of sleep apnea. For this reason, the endocrine society guidelines [20] recommends against the use of testosterone in patients with breast cancer, prostate cancer, unevaluated prostate nodule, unevaluated PSA elevation, hematocrit >50 %, Severe LUTS associated with AUA symptom score >19, and decompensated congestive heart failure. Patients should also be monitored regularly for efficacy of treatment and side effects. The Endocrine Society Guideline recommends evaluation of T level, hematocrit, PSA, bone mineral density on a regular interval as well as a history and physical to look for symptomatic changes. As we will discuss in the next section, there is emerging evidence that men >65 with multiple cardiovascular

co-morbidities may have increased cardiac events with T supplementation. See full guideline for more details [20].

The FDA has recently issued a "black box" warning regarding the possibility of transference of the T gel once applied by the patient to his body, to a partner or child. This can happen when the T gel is applied to an exposed skin surface and the patient comes into contact with the partner/child. The gels take about 2–6 h to dry once applied to the skin. This appropriate counseling must be provided to the patient when prescribing T replacement therapy [51, 53].

Treatment endpoints usually include T levels in the therapeutic range and relief of symptom(s). T levels can be raised to the higher therapeutic range if symptom relief is not accomplished with initial dosing regimens.

While T replacement therapy is contraindicated in men with known prostate cancer, there is a movement afoot to offer T replacement therapy to specific men who had undergone treatment for their prostate cancer. This is an extremely controversial area that is still under investigation [134, 166].

While T replacement is contraindicated in patients with AUA-SS >19 per the endocrine society guidelines, there have been multiple small studies showing that the use of T does not worsen LUTS and may actually improve LUTS [87, 166, 180]. However, good evidence is lacking and according to two recent systematic reviews, most studies looking at T replacement and LUTS used moderate-severe LUTS as exclusion criteria [87, 166]. There has also been evidence challenging the contraindication of T in patients with untreated OSA. Several small studies have shown that T was safely used in patients with untreated OSA, suggesting that OSA should not be an absolute contraindication [77, 94, 166].

Recent Developments in the Safety of Testosterone in Elderly Men

Testosterone usage in young men with symptomatic hypogonadism has never been in question – T use has provided benefits in terms of sexual function, mood, well-being, strength, BMD, bone quality, and secondary sexual characteristics with good safety profile in this patient population [179]. However, recent evidence has seriously questioned the safety profile of testosterone in age-related hypogonadism, especially in patients with minimally bothersome symptoms. These findings led the FDA to mandate testosterone product labels to clarify in the product labels that the "benefits and safety of these medications have not been established for the treatment of low testosterone levels due to aging" and "a possible increased risks of heart attacks and strokes in patients taking testosterone" [51, 53].

Older meta-analyses of several smaller RCTs showed that testosterone use in older men were not associated with increased cardiovascular events [24, 50]. However, recent data from the testosterone in older men "TOM" trial has created some concern regarding the cardiovascular risks of testosterone replacement in

older, more frail men with multiple baseline co-morbidities [12]. These authors studied community-dwelling men, 65 years of age or older, with limitations in mobility and a total serum T level of 100–350 ng/dl (3.5–12.1 nmol/l) or a free serum testosterone level less than 50 pg/ml (173 pmol/l). These men were randomly assigned to receive placebo gel or T gel, applied daily for 6 months. During the 6 months, 23 out of 106 patients in the treatment arm had a cardiac event compared to 5 of 103 in the control group. Included in those cardiac adverse events were death, stroke, MI, and syncope. Due to of the drastic difference in adverse events, the trial was stopped before recruitment was completed. This study also showed that patients on T gel had a higher rate of dermatologic events and any adverse event requiring referral. The authors concluded that in this population of older men with limitations in mobility and a high prevalence of chronic disease, the application of a testosterone gel was associated with an increased risk of cardiovascular adverse events.

In a retrospective cohort study, looked at men with testosterone <300 ng/dL who also underwent coronary angiography in the Veterans Affair (VA) health care system [193]. The adverse event profile of 1223 patients that were started on testosterone therapy after angiography was compared to 7486 patients who did not receive testosterone therapy using ICD-9 codes for myocardial infarction and ischemic stroke. Most of these subjects had multiple medical co-morbidities such as coronary artery disease (>50 %), hyperlipidemia (>80 %), diabetes (>50 %), and hyperlipidemia (>90 %). Even though patients who received testosterone therapy had less medical co-morbidities, there was a 1.29 HR ($P < 0.05$) of adverse cardiac events (ischemic strokes, myocardial infarctions, and death) at a 3 year-follow-up point. This study in the veteran population further supports the theory that use of testosterone in older men with cardiovascular co-morbidities may be risky.

Another large retrospective study investigated the use of testosterone and risk of non-fatal MI in the Truven Health MarketScan Commercial Claims and Encounters Database in the United States [58]. The incidence rate of MI 90 days after following the filling of a testosterone prescription (any formulary) was compared to incidence rate of MI for the 52 weeks prior filling the prescription based on ICD-9 codes. 167,279 total patients, including 25,767 patients older than 65 were included in the study. The overall post/pre prescription rate ratio (RR) of MI was 1.36 (95 % CI: 1.03–1.81). This RR was 2.19 (95 % CI: 1.27–3.77) for patients age > 65, compared to 1.15 (95 % CI: 0.83–1.59) for patients > 65 who were prescribed PDE-5 inhibitors instead. In men under 65, patients with a heart disease history had a significant RR of 2.07 (95 % CI: 1.05–4.11) compared to 0.91 (95 % CI: 0.60–1.37) in patients without a history of heart disease. The RR of PDE5-I was not significantly elevated in any patient population, suggesting that its safety profile was not affected by age or co-morbidities. However, as Seftel and Morgentaler [168] have pointed out, this study design was sub-optimal and subject to inaccurate reporting and bias.

To complicate matters further, recent Testosterone trials mentioned above [178] demonstrated that T replacement for 1 year had no statistically significant cardiovascular or prostatic risks. However, as the authors will admit, their study was not adequately powered to detect differences in adverse events and men with severe cardiac issues or prostatic issues were excluded. In their recent meta-analysis,

Seftel et al. did not find any level I studies to support an association between T replacement and CV disease [165].

While most evidence points suggest that there is a lack of evidence that T supplementation is dangerous in older men, the results of the TOM trial and the 2 large cohort studies should not be ignored. One must weigh the data presented in these trials with the evidence from the recent Testosterone Trials and earlier studies of testosterone's effects on CV symptom, mortality, and metabolic syndrome. Physicians must also carefully assess the nature of the patient's complaints and their overall medical picture to determine whether T supplementation is the best option. For example, patients with ED alone and a low T may be better suited for PDE5-I. Patients with complaints associated with vitality may not benefit from T replacement.

Ejaculatory Dysfunction

Ejaculatory dysfunction in the aging male can be manifest as either rapid or delayed ejaculation. Both entities are difficult to quantitate epidemiologically. Delayed ejaculation, (which is not well -defined in terms of time), in the aging male is most likely a combination of neuropathy of the ejaculatory pathway and a change in the prostatic milieu. The neuropathy may result from diabetes, vitamin deficiency, anatomic spine issues, CNS issues, thyroid issues, post transurethral resection of the prostate, any pelvic surgery that affects the pelvic nerves (i.e., radical prostatectomy), or combinations thereof. The prostate is predominately a reproductive organ in the young man, and turns into a less glandular, more fibrotic organ with aging, and thus is less secretory. This may result in "delayed" ejaculation. Delayed ejaculation is thought to be psychogenic in origin in younger men and organic in older men. In general, delayed ejaculation is challenging to treat, as many of the disease processes noted above are chronic, rendering correction of the delayed ejaculation less likely.

Premature ejaculation in the aging male is also enigmatic [196]. The definition of premature ejaculation is somewhat elusive as worldwide studies reflect the disparity in the "normal" ejaculatory period [197]. In a large, multinational study, the intravaginal ejaculatory latency time (the IELT, which is the sine qua non measurement for rapid ejaculation) had a mean of 5.7 min and a median of 6.0 min (range: 0.1–52.1 min). Men from Turkey had the shortest median IELT (4.4 min). Men from the United Kingdom had the longest IELT (10.0 min). Circumcision and condom use had no significant impact on the median IELT. Subjects who were discontent with their latency time had slightly lower median IELT of 5.2 min compared to the median of the population.

Premature or rapid ejaculation has been historically defined by time as ejaculation 1–2 min of erections. The current definition consists of rapid ejaculation combined with distress. This definition of rapid ejaculation can be independent of vaginal penetration, in spite of the fact that intravaginal latency time is used as the barometer of rapid ejaculation [2].

Premature ejaculation (PE) is a very common sexual dysfunction among patients, and with varying prevalence estimates ranging from 3 to 20 % [148]. Please recall the following data discussed earlier. In a younger cohort of men and women in the National Health and Social Life Survey, 31 % of men have some sexual dysfunction with the most frequent being ejaculatory dysfunction [195].

Rapid ejaculation may be a response to erectile dysfunction and may therefore correct itself once the ED is corrected. Alternatively, rapid ejaculation may be lifelong and may only rise to the surface as a problem for the aging male. Rapid ejaculation is thought to be in part genetic in the young man. In one population-based sample of 1196 Finnish male, there was a moderate genetic influence (28 %) in rapid ejaculation in twins age 33–43 years [81]. This genetic relationship has not been established in the aging male.

Diagnosis of Ejaculatory Dysfunction

The diagnosis of ejaculatory dysfunction in the male is based upon history. The questionnaires mentioned above may be as well [159–161]. Rapid ejaculation and delayed ejaculation remain challenging areas for the clinician.

Treatment of Ejaculatory Dysfunction

With increasing interest and clinical research in male sexual disorders, it has become clear that not only psychological but also organic, neurobiological, and genetic factors may play an important role in premature ejaculation (PE [148],). Although psychological issues are present in most patients with premature PE, effects of psychological approaches for PE is not well-studied and lacks long-term data based on a recent Cochrane [128]. The authors noted that there was weak and inconsistent evidence regarding the effectiveness of psychological interventions for the treatment of PE. Three of the four RCTs reported our primary outcome (Improvement in IELT). Most of the studies had a small sample size. The early success rate of Masters and Johnson (97.8 %) could not be replicated. One study found a significant improvement from baseline in the duration of intercourse, sexual satisfaction and sexual function, and behavior therapy compared to patients on a waiting list. One study showed that the combination of chlorpromazine and behavioral therapy was superior to chlorpromazine alone. Randomized trials with larger group samples are needed define the role of psychological interventions for treating PE.

FDA- approved oral therapy for PE is currently not available. Dapoxetine was studied several years ago as a potential option [126]. Dapoxetine, a potent SSRI, is administered on demand 1–3 h before planned sexual contact. Dapoxetine 30 and 60 mg has been evaluated in five double-blind, placebo-controlled RCTs studies involving 6081 ≥ 18 years old. Outcome measures included stopwatch-measured

IELT, Premature Ejaculation Profile (PEP) items, clinical global impression of change (CGIC) in PE, and adverse events. Mean IELT, all PEP items and CGIC improved significantly with both doses of dapoxetine versus placebo ($p<0.001$ for all parameters). The most common adverse events were nausea, dizziness, and headaches. Evaluation of validated rated scales demonstrated no SSRI class-related effects with dapoxetine use [30]. Dapoxetine did not receive FDA approval for use in the US but has received approved in several other countries.

Ejaculatory dysfunction can also be caused by an underlying medical condition or medication. In those cases, treatment would involve reversing the underlying etiology. For example, hypogonadism may cause delayed ejaculation, in which case a patient should consider testosterone replacement after extensive discussion about the risks and benefits of testosterone therapy (see above). If retrograde ejaculation due to α-blockers is bothersome, a patient should reconsider his BPH/LUTS regimen.

STDs in Aging Populations

Sexually transmitted disease has become more prevalent as people get older and reengage in sexual activity. According to a CDC report in 2009, the percent of patients presenting for care of HIV increased who were greater than 50 years old increased from 17 % in 1997 to 27 % in 2007 [23]. Although HIV/AIDS transmission through blood transfusions has decreased, other sources of cases by sexual intercourse and multiple sexual partners have increased the number of documented cases [185]. Risk factors for HIV/AIDS in the aging population are the same as those for younger adults – sexual contact, multiple partners, STDs, substance abuse, and intravenous drug use. Based on a 2008 National Survey of Sexual Health and Behavior, in people age greater than 50 years of age, a condom was not used in sexual intercourse with 91.5 % of casual partners, 76.0 % of friends, 69.6 % of new acquaintances, and 33.3 % of transactional sexual partners [116].

Older people are especially prone to the sequelae of HIV/AIDS largely because of the decline of humoral and cell-mediated defense mechanisms associated with the aging process [40, 62]. The geriatric population is more susceptible to opportunistic infections such as mycobacterium tuberculosis, herpes zoster, and cytomegalovirus. Post-menopausal women as especially at risk for contracting HIV during sexual intercourse because of decreased lubrication and vaginal wall thinning [86, 172, 205]. There is a more aggressive pattern of progression after HIV seroconversion with a lesser response to antiretroviral treatment agents. There are also additional comorbidities that the elderly have predisposes them to an early and rapid demise once afflicted with AIDS as multiple systems are compromised quicker. In fact many elderly die of AIDS before a diagnosis of HIV infection is even made [86, 172, 205].

Treatment of HIV/AIDS in elderly patients is the same as in the general population. There is a greater propensity for interactions and adverse reactions

because older people are usually taking additional medications for their comorbidities. In older adults, antiretroviral therapies should be started at low dosage and increased gradually under close monitoring. Unfortunately, this patient population has the burden of combined compromised health and compromised cognitive ability to adequately deal with the initial diagnosis of HIV and the physical and emotional stress of going through the treatment plan [108]. Elderly patients diagnose with HIV/AIDS require additional support as well as a discussion weighing the risks and benefits of HIV/AIDS treatment in the context of end of life issues.

Because of the significant risks of HIV and other STDs in the geriatric population, it should be stressed to older adults that age in and of itself is not a barrier against these diseases. In the older patient who experiences memory loss, a workup for syphilis should be conducted in additional to evaluating for other neurologic conditions [172, 205]. Other more common STDs such as gonococcal urethritis, vaginitis, trichomoniasis, and Chlamydia, are as ubiquitous amongst the geriatric population as its younger counterpart and should be appropriately treated when found [156]. In nursing homes and assisted living facilities, sexual assault of the cognitively impaired individual should be considered if he or she develops STDs [172, 205]. These various issues and statistics underscore the importance of affirming safe sexual practices amongst the geriatric population by the general practitioner.

Comorbidities

Comorbid disease processes can have a significant negative impact on sexual health, especially in the geriatric population. Disease states usually cause low energy levels, fatigue, pain, impairment, muscle weakness, and psychologic disturbances that hamper a sexual relationship [86, 136]. Conditions requiring surgical intervention can affect anatomic functions (e.g., amputations, colostomy, urostomy, etc.) and distort self-image (e.g., scars, burns) and lower self-esteem, causing problems with sexual attraction [86]. Often times, patients refrain from significant sexual contact even after the resolution of a disease state. Examples include the post-prostatectomy patient as the patient may be unable to get an erection or the post-myocardial infarction (MI) patient because he or she is fearful of getting a second MI during intercourse. Updated guidelines for the clinician have recently been published to assist with the post MI patient and other patients afflicted with CV disease who wish to resume sexual activity [98, 111, 131]. A cardiovascular evaluation may be required to assess the patients' physical capability and cardiovascular requirements necessary to resume sexual intercourse. Both sexual partners should be cognizant and comfortable with sexual activities after one partner undergoes a life altering condition or surgery.

Post-CVA patients may have paralysis or reduced libido and diminished orgasms. Post-stroke weakness can be unilateral and can sometimes be addressed

by alternative positioning while engaging in sexual activities [86, 136]). Concerns also exist that medications used to treat certain conditions may result in sexual dysfunction.

Diabetes, a significant contributing factor for ED in men, can also negatively impact women's sexuality. DM can cause a decrease of vaginal secretions and reduce libido. Different sequelae of DM such as retinopathy leading to blindness, amputations, renal failure requiring dialysis, peripheral neuropathy, and chronic pain can all hamper sexual functioning [62]. Chronic arthritis can cause pain and joint swelling, limiting range of motion during sex [85].

Postsurgical patients, including all forms of surgery, may experience side effects such as pain, scarring, and lymphedema, all of which can interfere with a patient's desire and ability to engage in sexual activities. The patient's partner may also find it difficult to cope with his or her partner's sexual difficulties and inadequacies and may not feel any sexual attraction under those circumstances [86, 136]. There is a heavy toll on both the physical and emotional components of post-surgical relationship. Most post-hysterectomy women found less desire and enjoyment during intercourse after their surgeries; however, a minority had improved sexual activity because their pre-hysterectomy symptoms and pain were gone [67].

In men, the most common non-cutaneous malignancy is prostate cancer. With any of the treatment modalities offered, including open or robotic radical prostatectomy, external beam radiation, or brachytherapy, there is significant concern for incontinence, impotence, and diminished libido [83]. Prostatectomy, if not nerve-sparing, may inhibit return of spontaneous erections. In addition, some men consider prostatectomy as an assault on his male sexuality and suffer considerable psychological detriment post-operatively, thereby diminishing sexual desire and function [4]. Urinary incontinence as a result of radical prostatectomy can also impact sexual behavior negatively in the elderly. Nocturia, bedwetting, fear of incontinence during sex can all decrease sexual desire and activity. The use of Kegel exercises to improve continence and appropriate medications can sometimes overcome these side effects and may lead to improvement in sexual function in an older man [120]. The post –prostatectomy male has the same options for the treatment of erectile dysfunction listed above for the elderly patient.

In addition to organic comorbidities, one must consider chronic psychologic disease as associated with sexual dysfunction. Depression and anxiety are serious and prevalent disorders in American men and women [105]. Like the story of the chicken and the egg, depression and anxiety can precede and cause sexual dysfunction as well as be a result of sexual dysfunction. Although psychotherapy and pharmacotherapy can provide substantial relief and clinical improvement in disease extent, some antidepressants have sexual side effects, making these drugs counterproductive in treating sexual dysfunction.

Religious and Cultural Aspects

In the aging population, many of the tenets and religious philosophies taught to them in their childhood play a significant role in their adulthood. Some cultures paint sexuality and its expression as a picture of sin and darkness on a religious basis. Others allow for more freedom and insight. In some settings, prior religious teachings can detract the elderly from experiencing a satisfactory sexual relationship because of feelings of guilt and repression. It is therefore important for urologists and physicians to address these religious feelings and attempt to incorporate the treatment of sexual dysfunction in a manner that is understanding of and complementary to the patient's religious background [76].

Conclusions

In summary, sexuality still plays a predominant role in the health and general well-being of the older adult. There are a multitude of physical, psychological, emotional, and spiritual implications of a healthy sex life as men and women age [96]. A healthy sense of sexuality in the aging adult provides a more fulfilled lifestyle and significantly improves quality of life. Although there are challenges and diseases that can affect sexuality as one age, those obstacles can be treated and sometimes overcome outright. As more and more Americans live longer, it becomes increasingly more important that the urologist and general practitioner come to terms with the fact that sex life does not disappear with old age and that many elderly people have and enjoy a satisfactory sexual experience. With a balanced and healthy lifestyle, optimal treatment for medical conditions, advances and medical breakthroughs, sexual well-being is within reach of all with advanced age.

Epilogue

The authors are indebted to the numerous researchers who have contributed to this field. This chapter reflects their significant time commitment to the field of sexual medicine.

The keys to success in this discipline are to remember that these patients are a distinctive group that requires understanding and patience to help them achieve their goals.

Older folks face unique challenges that while not exclusive to their age group, are certainly more common to their age-group, such as sexual dysfunction, loss of

partner, cognitive impairment, fragility, mobility issues, and cardiovascular disease. Hormonal therapies have come under scrutiny as data has emerged that has suggested that hormonal replacement may have negative consequences, creating uncertainty as to how to evaluate and treat the hormonally-deficient older male and female. Treatment of sexual dysfunction is adapted from the literature that delineates treatment options for a cohort in the lower age range of seniority (50's and 60's). The application of these treatments to the older patient requires thoughtfulness and an understanding of the needs of the individuals. Societal mores often place the older patient into an uncomfortable position, as the patient, who may be seen as either the patriarch or matriarch of the family, may be viewed with some disdain by loved ones as they re-engage in sexual activities thought to be in the domain of the young. The clinician must integrate a wealth of knowledge and combine that with finesse, caring, and compassion, all in a non-judgmental manner to be an effective advocate for these patients. It is our hope that we have been of some assistance in helping both the clinician and patient meet their goals.

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